



October 16 - 18
14th EDITION **2015**

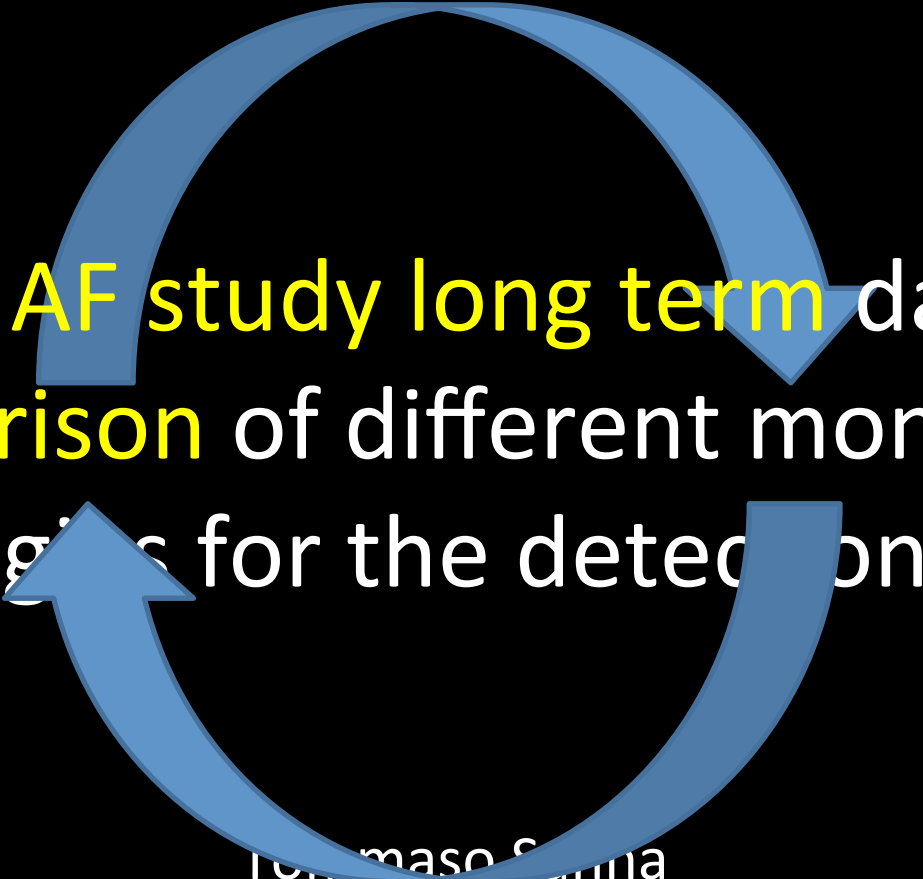
MY CONFLICTS OF INTEREST ARE:



- **Consultant Medtronic Inc**
- **Speakers fee from Boheringer Ingelheim**

Crystal AF study long term data and comparison of different monitoring strategies for the detection of AF

Tommaso Sanna
UCSC Rome, Italy



Crystal AF study long term data and
comparison of different monitoring
strategies for the detection of AF

Tommaso Santina
UCSC Rome, Italy

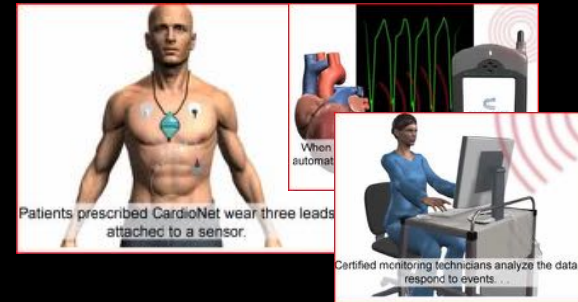
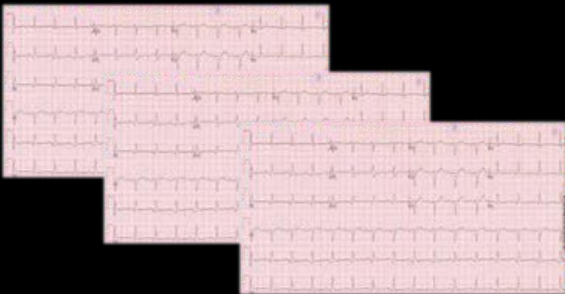
Comparison of different monitoring strategies for the detection of AF and **Crystal AF study long term** data

Tommaso Sanna
UCSC Rome, Italy

Diagnostic tools



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AF after ischemic stroke

Atrial fibrillation detected by mobile cardiac outpatient telemetry in cryptogenic TIA or stroke

Detection of Paroxysmal Atrial Fibrillation by 30-Day Event Monitoring in Cryptogenic Ischemic Stroke
The Stroke and Monitoring for PAF in Real Time (SMART) Registry
Alexander C. Flint, MD, PhD; Nader M. Banki, MD; Vivek A. Rao, MD; Alan S. G...

THE NEW ENGLAND JOURNAL OF MEDICINE
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Randomized Trial of Outpatient Cardiac Monitoring After Cryptogenic Stroke
Kamel, MD; Babak B. Navi, MD; Lucas Eljovich, MD; S. Andrew Josephson, MD; Yee, DO; Gordon Fung, MD; S. Claiborne Johnston, MD, PhD; Wade S. Smith, MD, PhD

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?

Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis

Luciano A Sposato, Lauren E Cipriano, Gustavo Saposnik, Estefania Ruíz Vargas, Patricia M Riccio, Vladimir Hachinski

Lancet Neurol 2015; 14: 377–87



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Phase 1: Admission



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Admission ECG

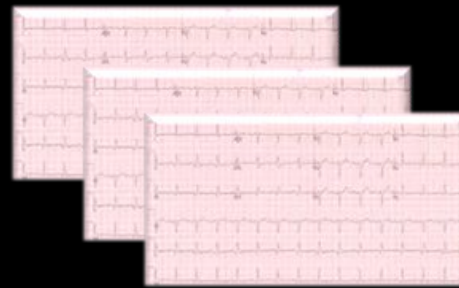
Phase 2: In-hospital

Serial ECG



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In-hospital telemetry



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In-hospital
bedside monitoring



In-hospital Holter monitoring

Phase 3: After discharge (short term)



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Outpatient Holter monitoring

Phase 4: after discharge (long term)



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Mobile Cardiac
Outpatient Telemetry



Event recorders



Implantable Cardiac Monitor

AF after ischemic stroke

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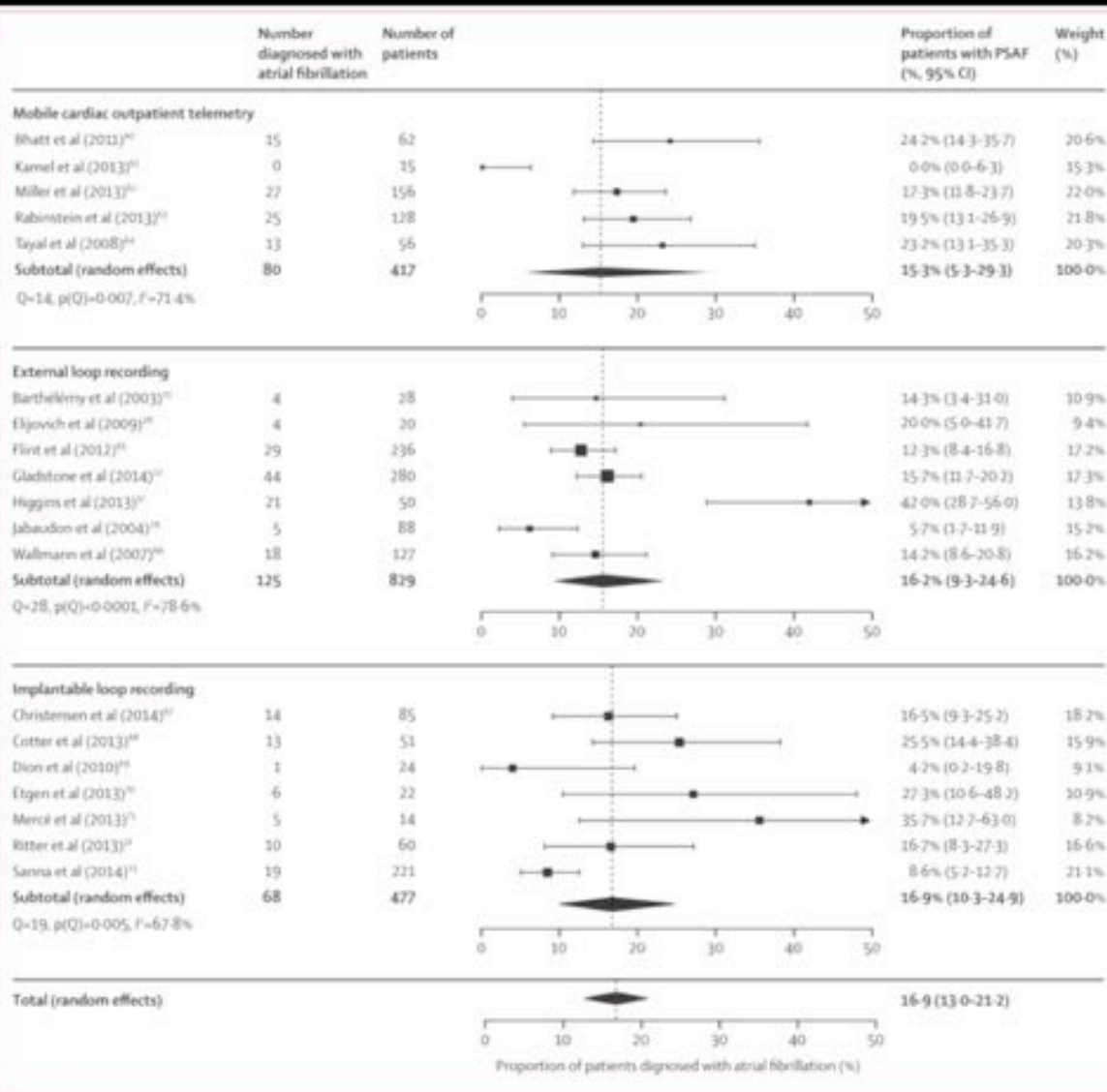
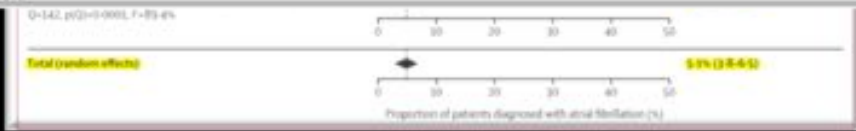


Figure 5: Proportion of patients diagnosed with post-stroke atrial fibrillation during phase 4 (second ambulatory period) PSAF=post-stroke atrial fibrillation.



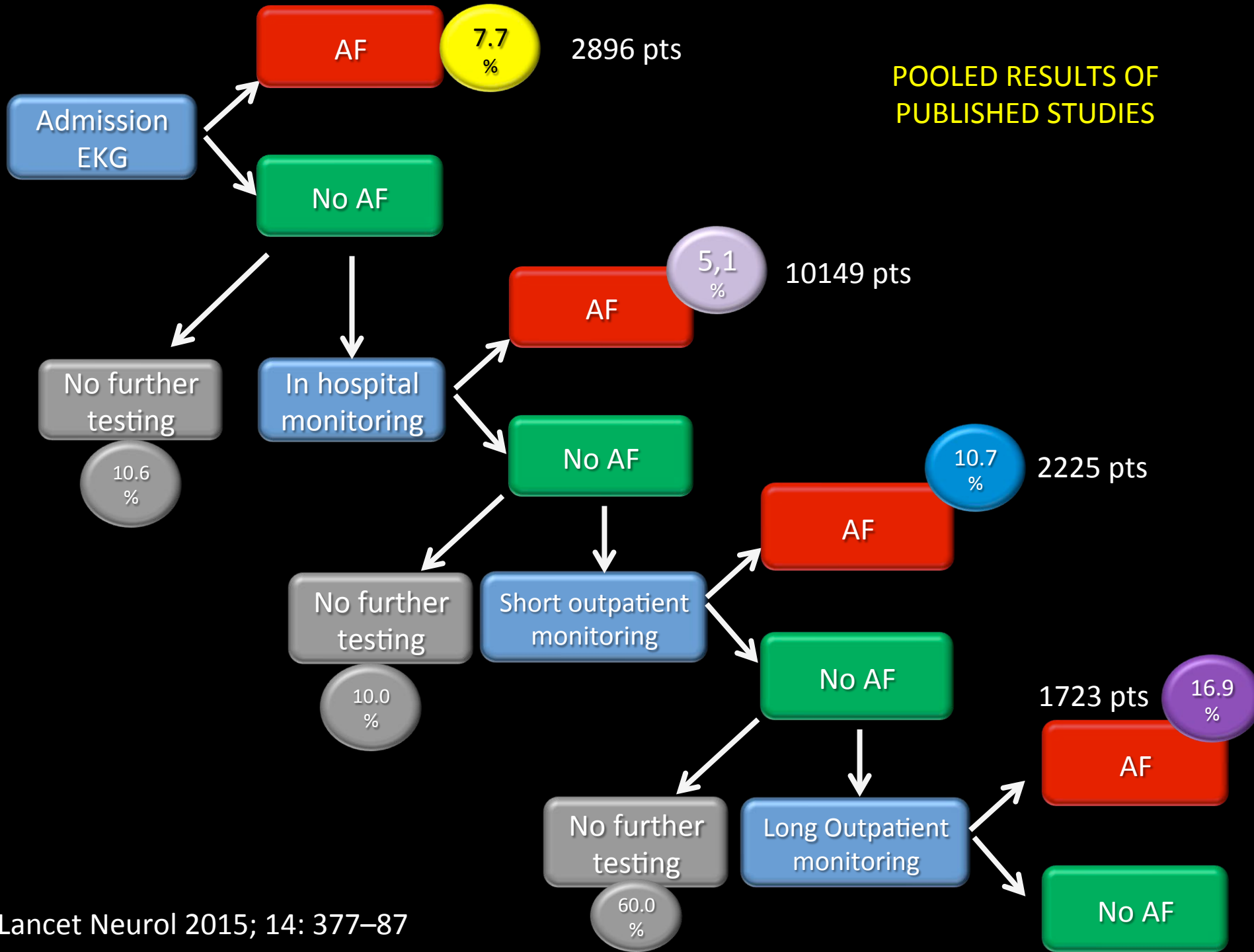
Ambulat
Alhadram
Dangayak
Doliwa et
Forneca e
Gunalp e
Marina e
Ritter et
Schucher
Shafiqat e
Shibazaki
Tagawa e
Vanderbr
Yodogawa
Subtotal
Q=148, p

Figure 4: P
PSAF=post
monitoring

Proportion of patients with PSAF (% 95% CI)	Weight (%)
4.7% (1.6-9.3)	8.5%
1.7% (0.1-8.2)	5.6%
8.1% (5.6-10.9)	10.1%
5.2% (2.0-9.8)	8.6%
4.1% (1.9-7.3)	9.4%
2.7% (0.6-6.3)	8.6%
9.6% (6.4-13.4)	9.7%
12.9% (10.6-15.3)	10.5%
16.2% (11.7-21.2)	9.5%
6.2% (3.6-9.5)	9.7%
15.7% (11.6-20.2)	9.8%
7.7% (5.0-10.8)	100.0%

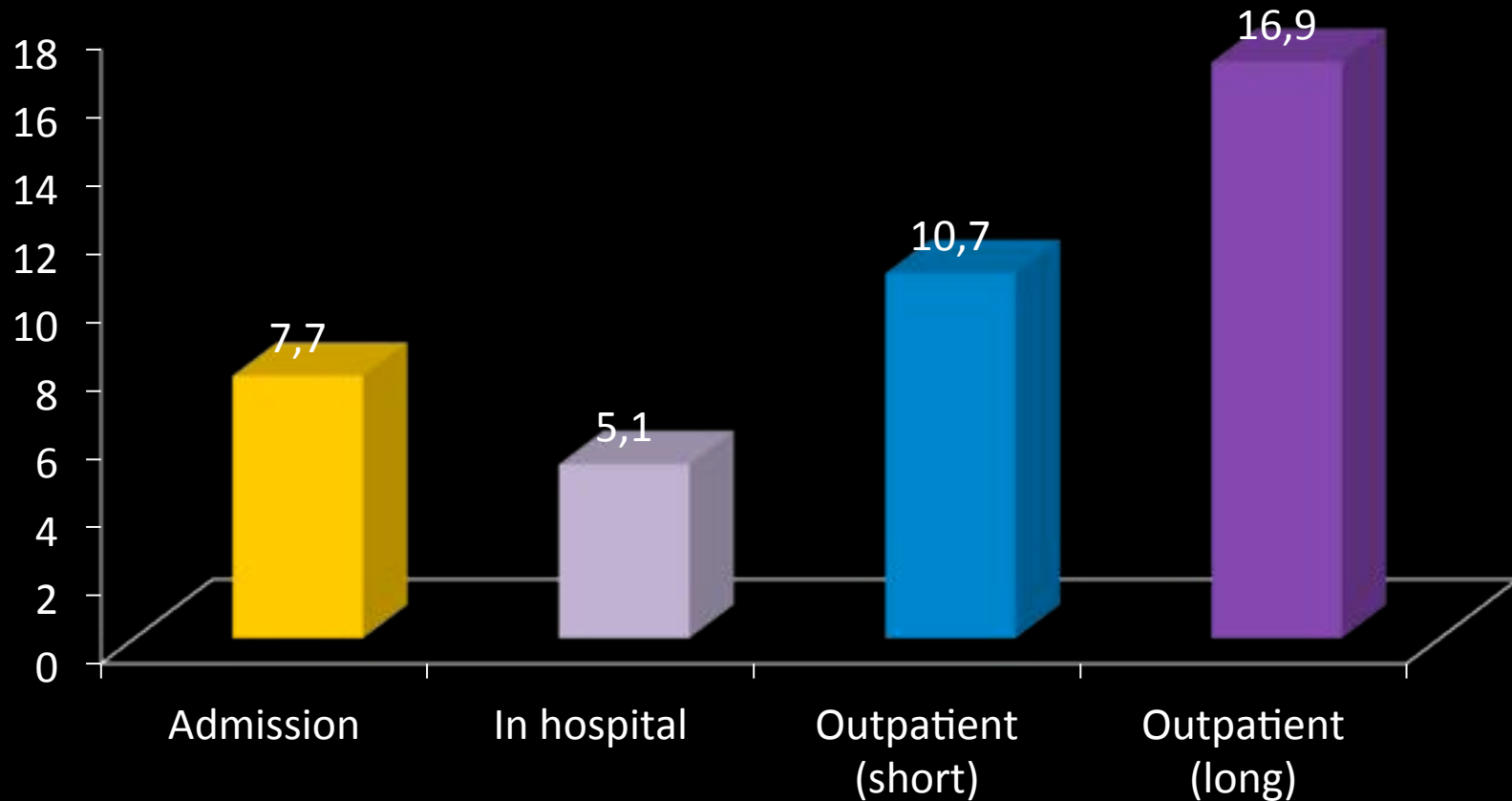
50
(%)
ity room)

POOLED RESULTS OF PUBLISHED STUDIES

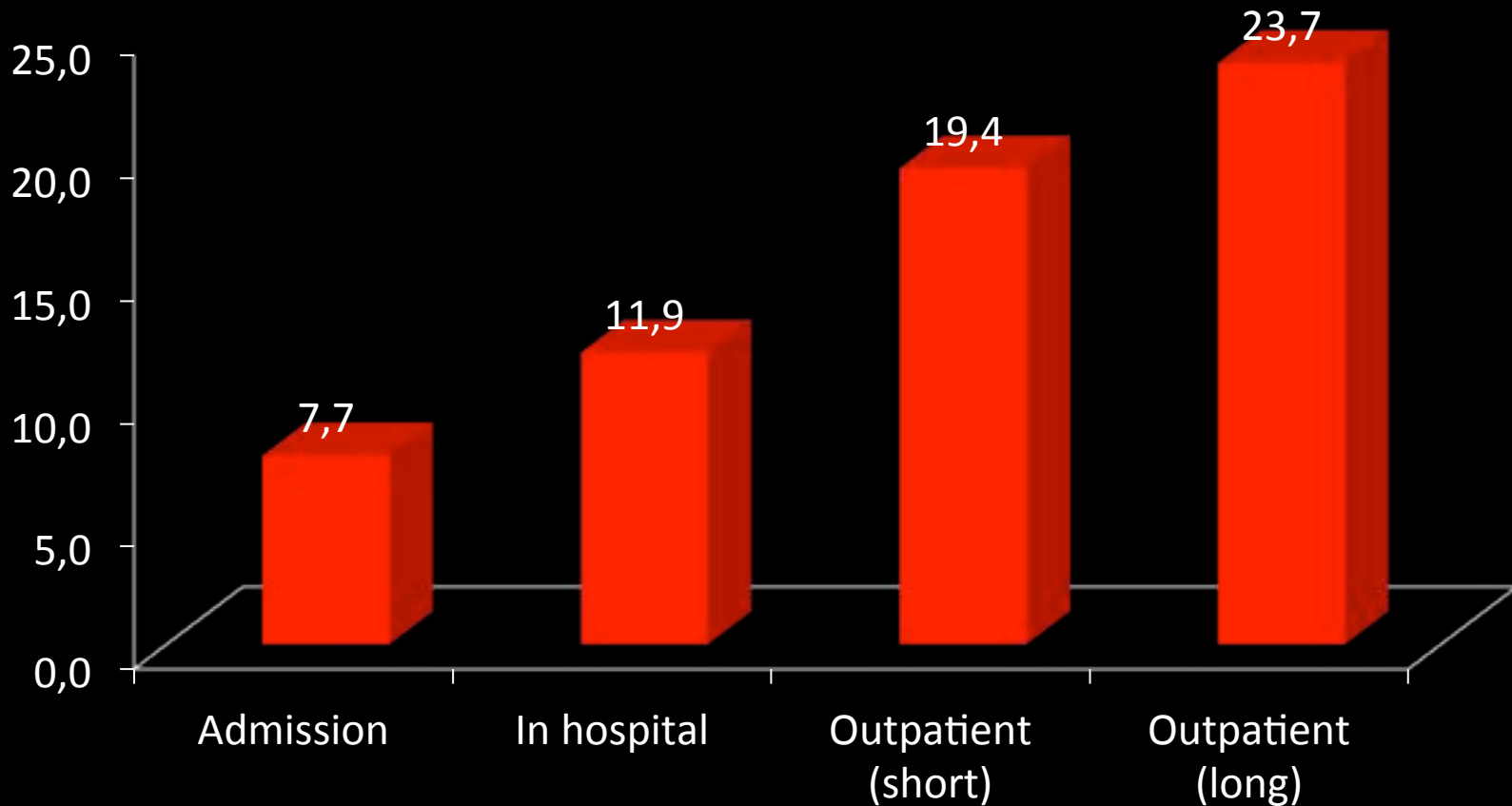


New AF detection at each phase

Pooled % of pts with no history of AF among those undergoing monitoring



Cumulative AF detection at 180 days with sequential monitoring



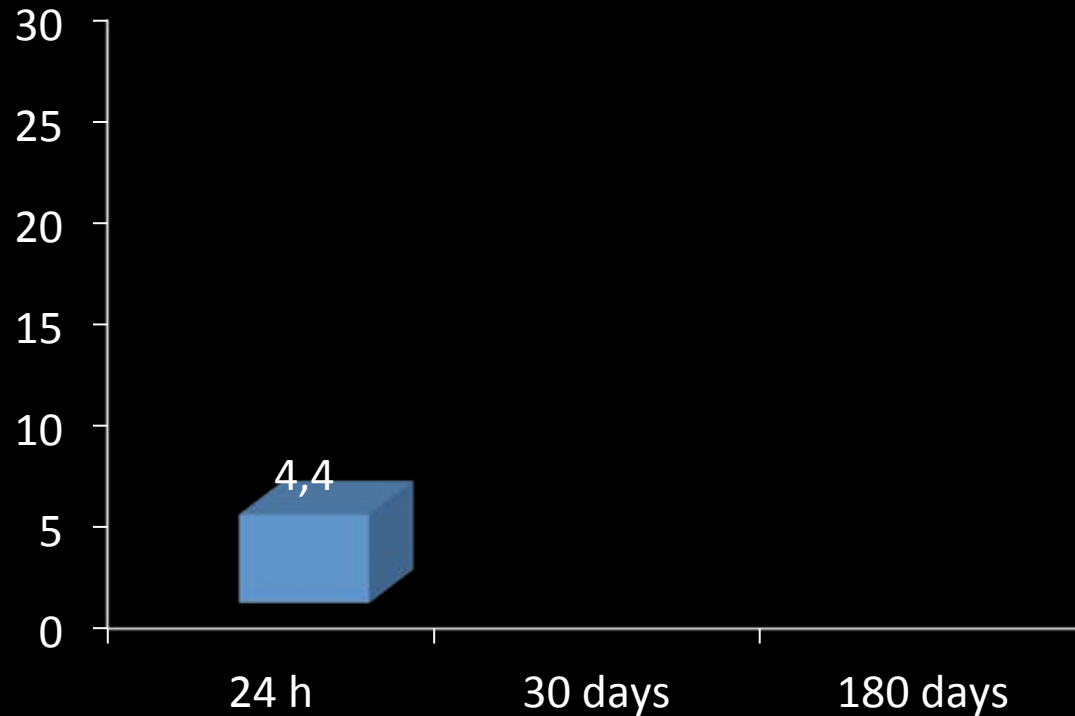
Original Article

Electrocardiographic Monitoring for Detecting Atrial Fibrillation After Ischemic Stroke or Transient Ischemic Attack Systematic Review and Meta-Analysis

Charles Dussault, MD; Hadi Toeg, MD, MSc; Meena Nathan, MD; Zhi Jian Wang, MD;
Jean-Francois Roux, MD; Eric Secemsky, MD

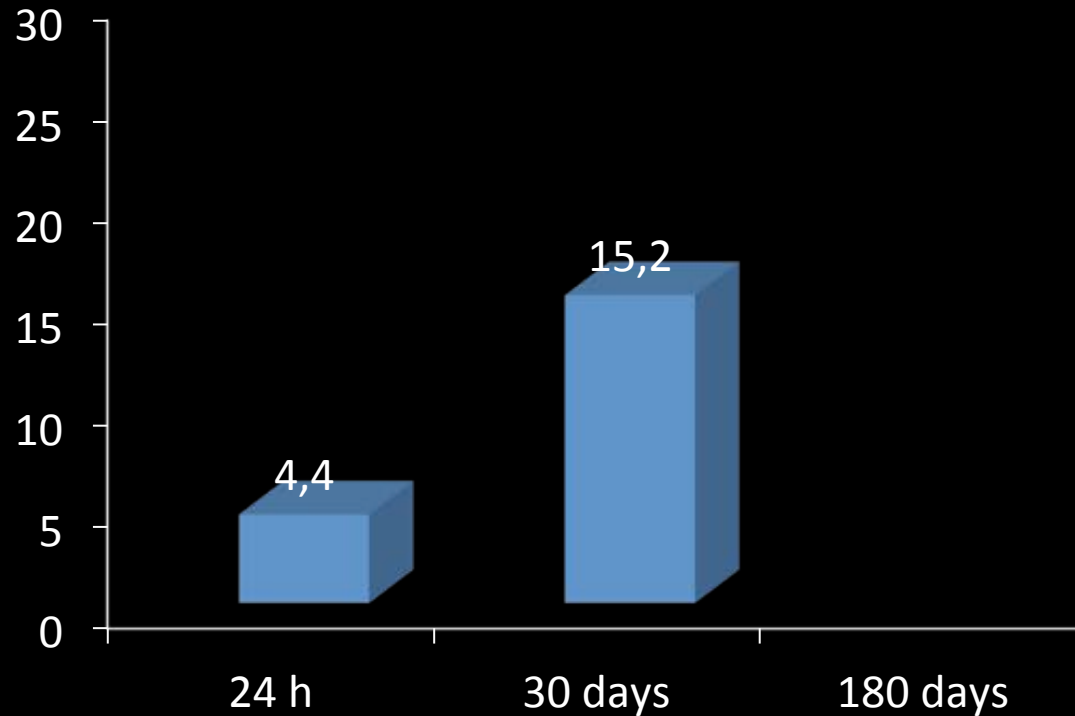
(Circ Arrhythm Electrophysiol. 2015;8:263-269)

AF detection after ischemic stroke



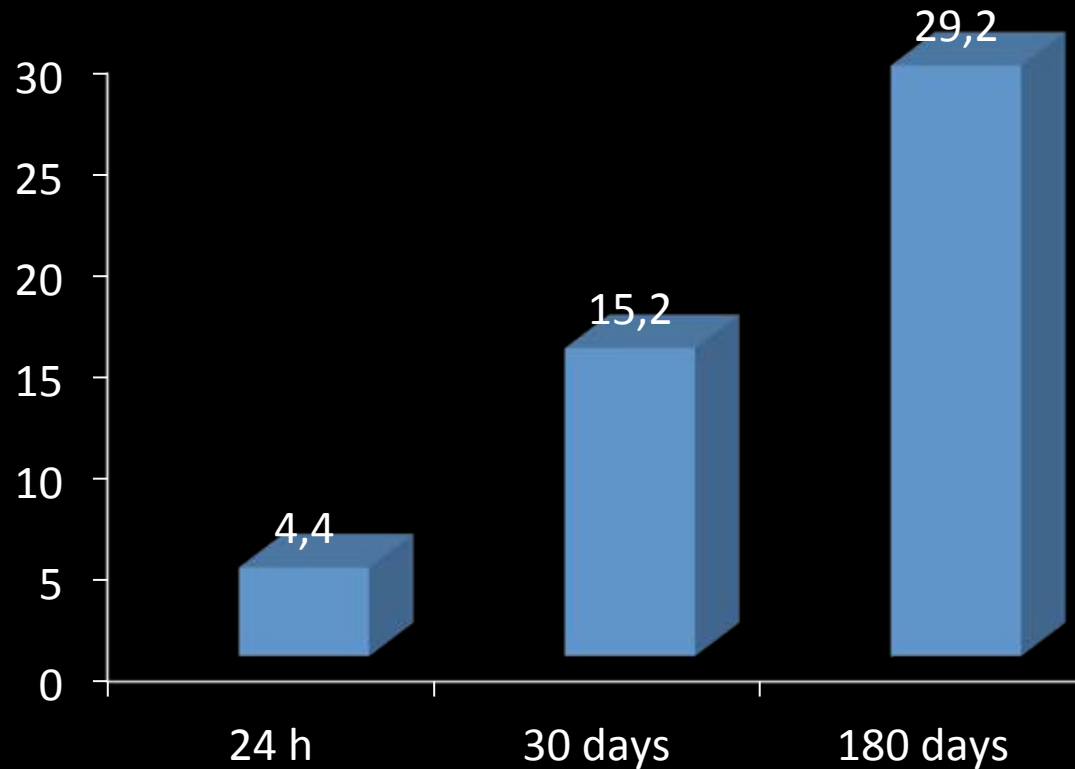
(Circ Arrhythm Electrophysiol. 2015;8:263-269)

AF detection after ischemic stroke

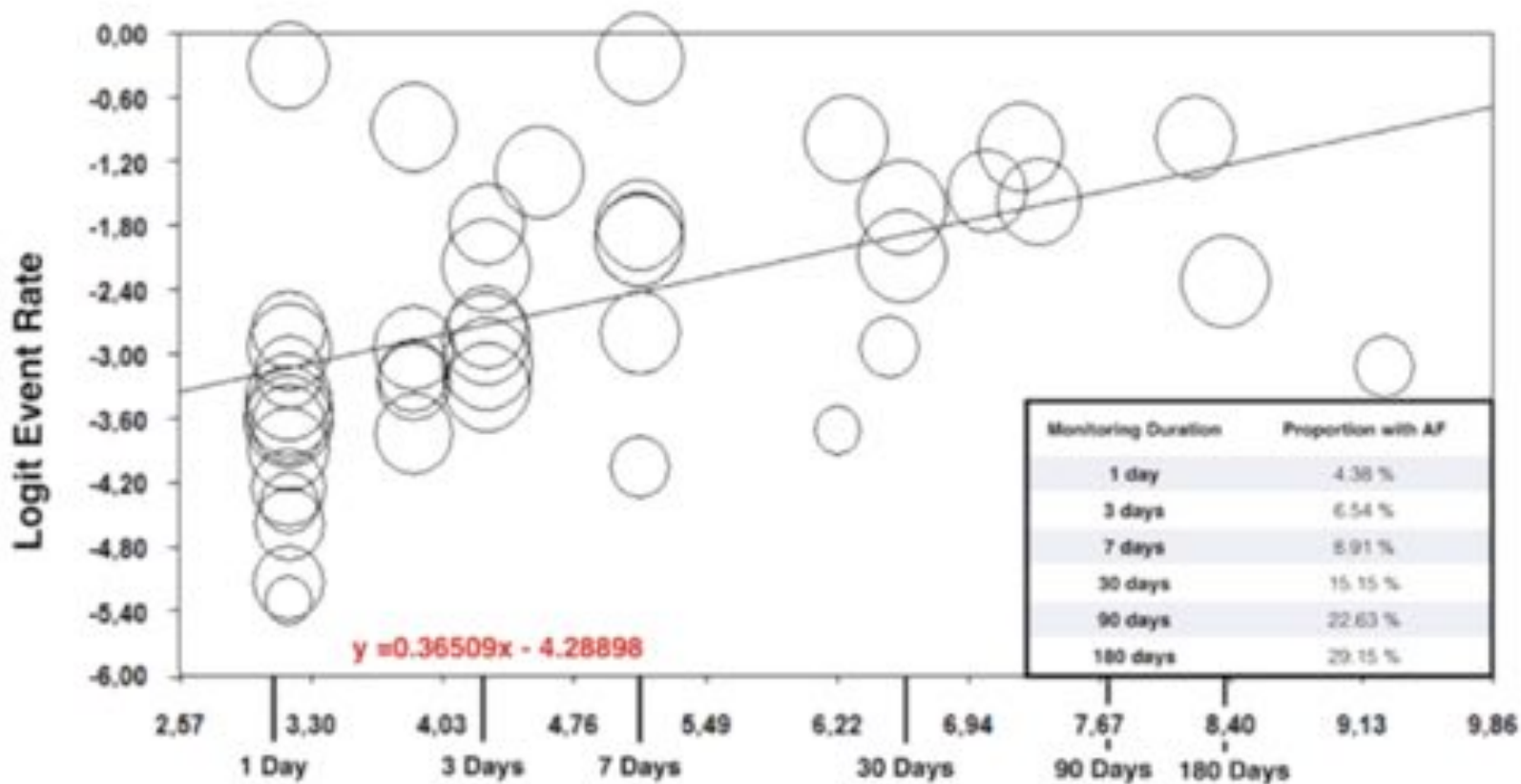


(Circ Arrhythm Electrophysiol. 2015;8:263-269)

AF detection after ischemic stroke



(Circ Arrhythm Electrophysiol. 2015;8:263-269)



(Circ Arrhythm Electrophysiol. 2015;8:263-269)

The more you search
the more atrial fibrillation you find

Heterogeneity

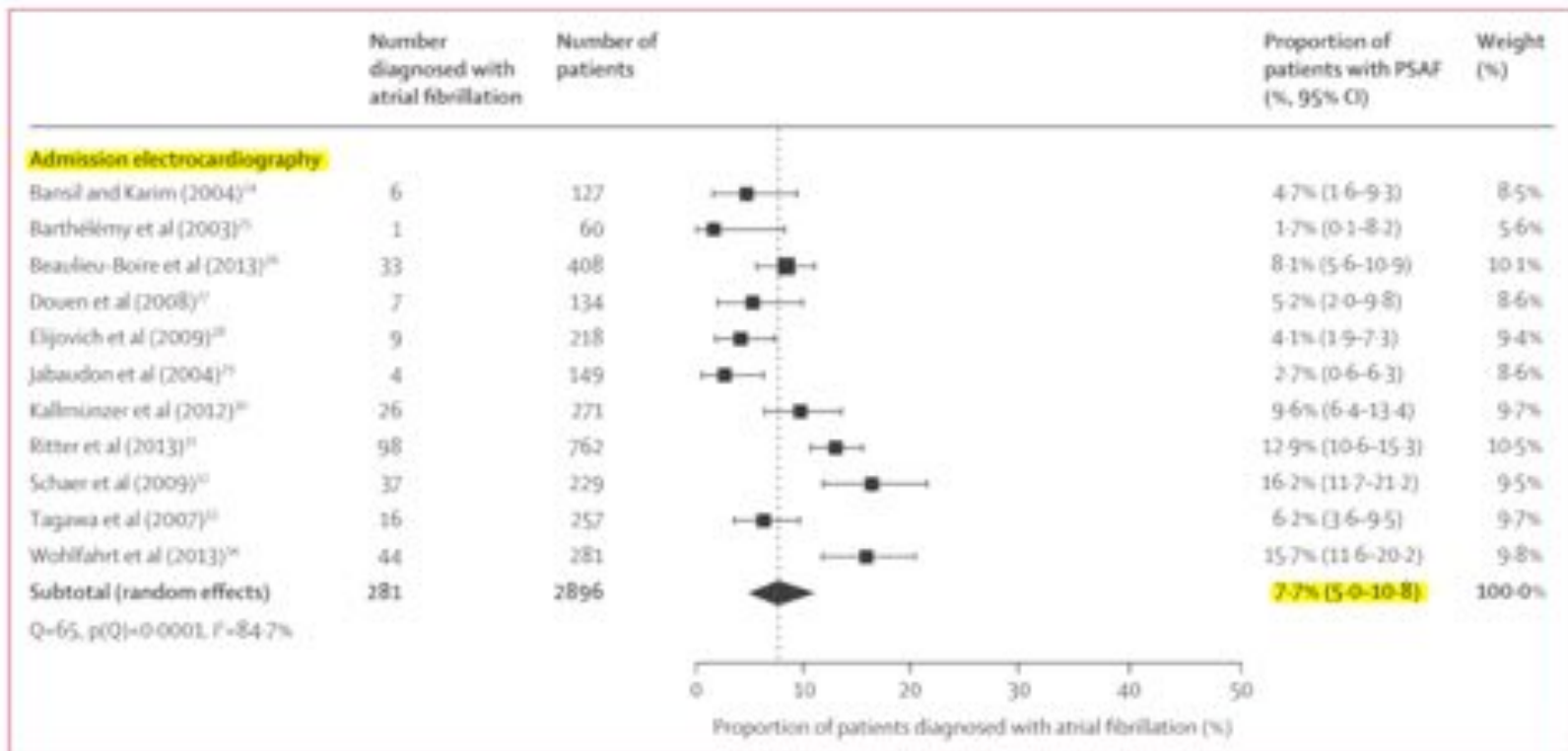
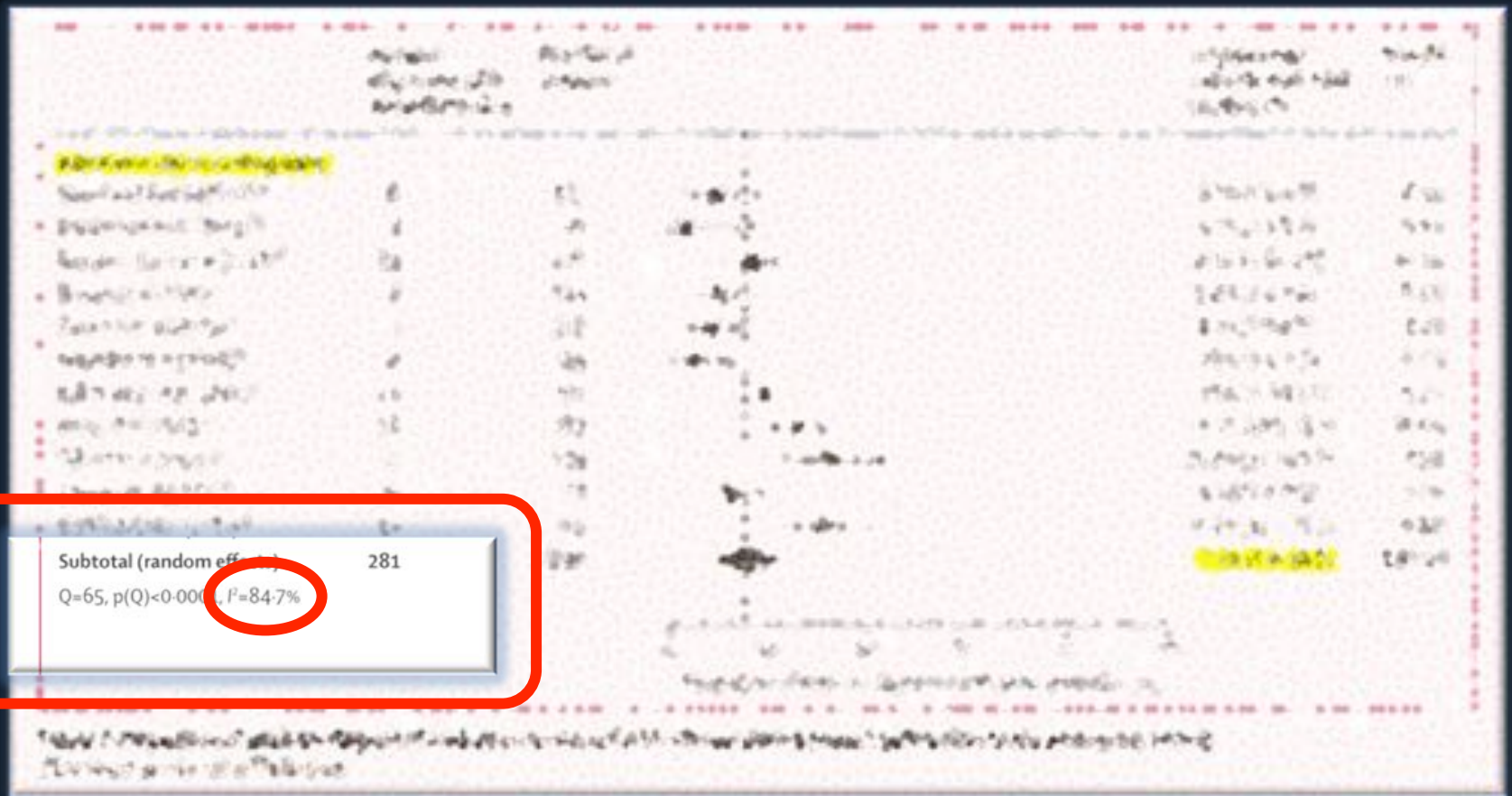
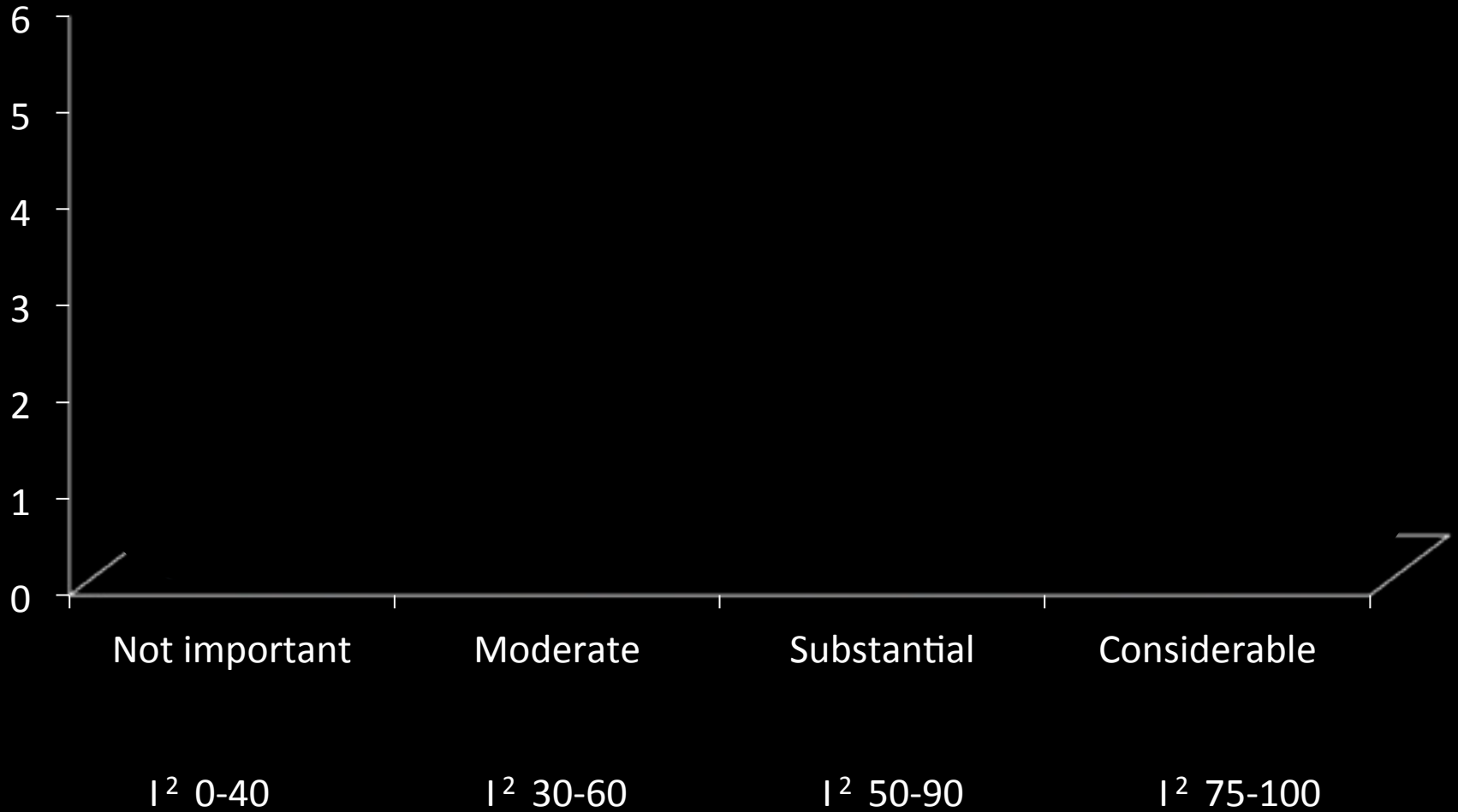


Figure 2: Proportion of patients diagnosed with post-stroke atrial fibrillation during phase 1 (admission to the emergency room)
PSAF= post-stroke atrial fibrillation.

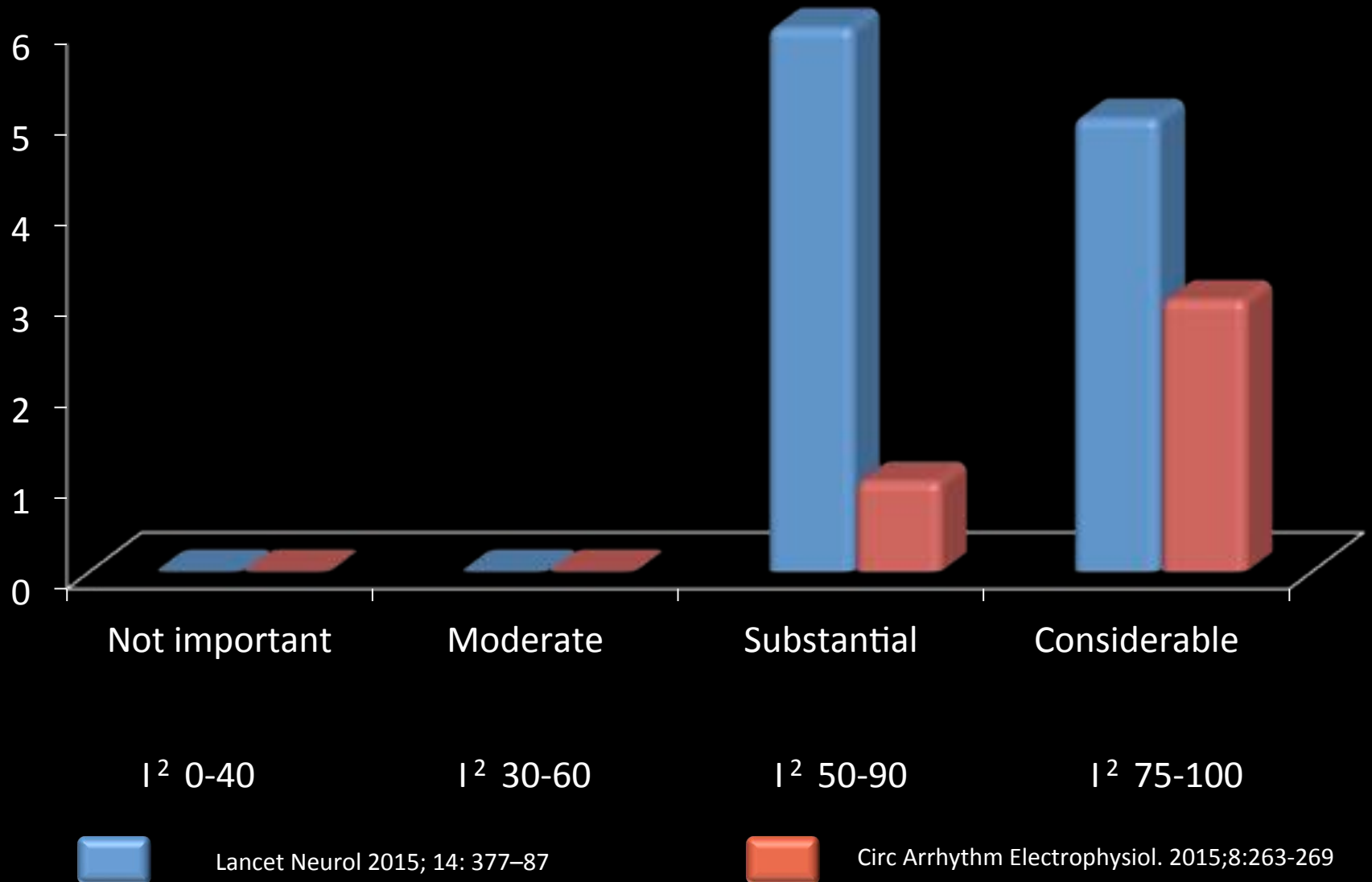
Heterogeneity



Heterogeneity



Heterogeneity





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Spot the differences !



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1

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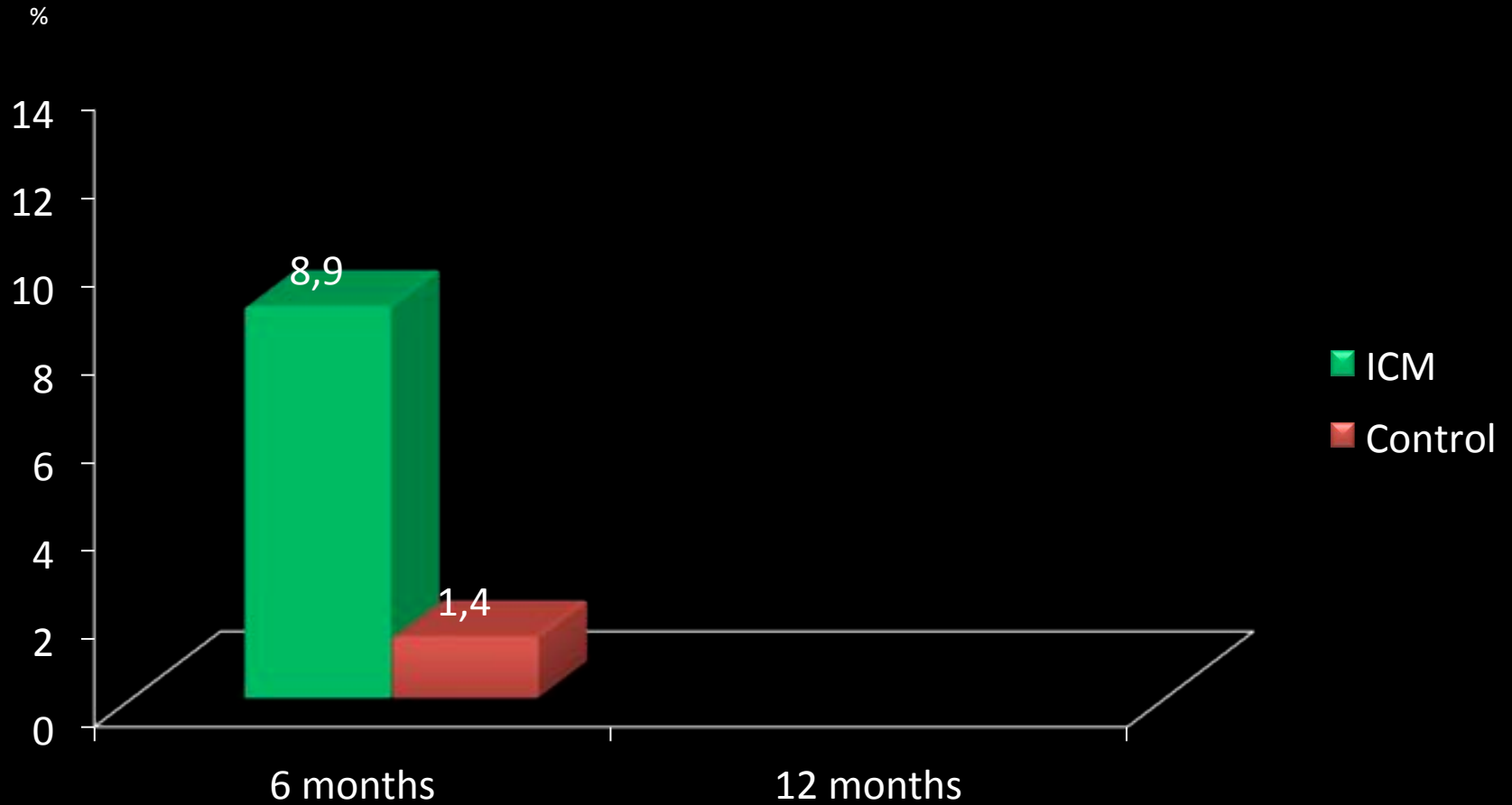
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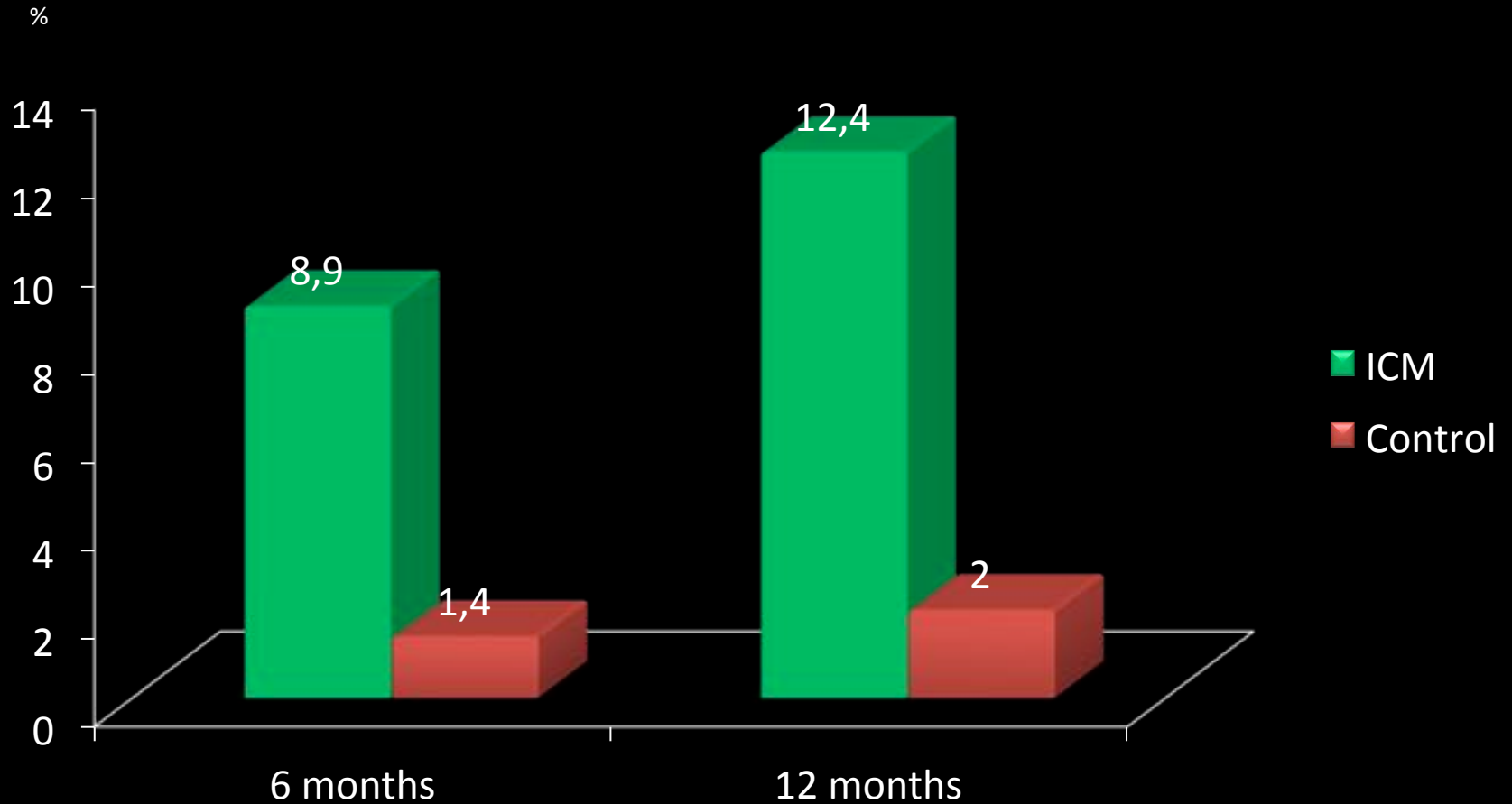
Atrial fibrillation detection

Atrial fibrillation detection



N Engl J Med 2014;370:2478-86.

Atrial fibrillation detection



N Engl J Med 2014;370:2478-86.

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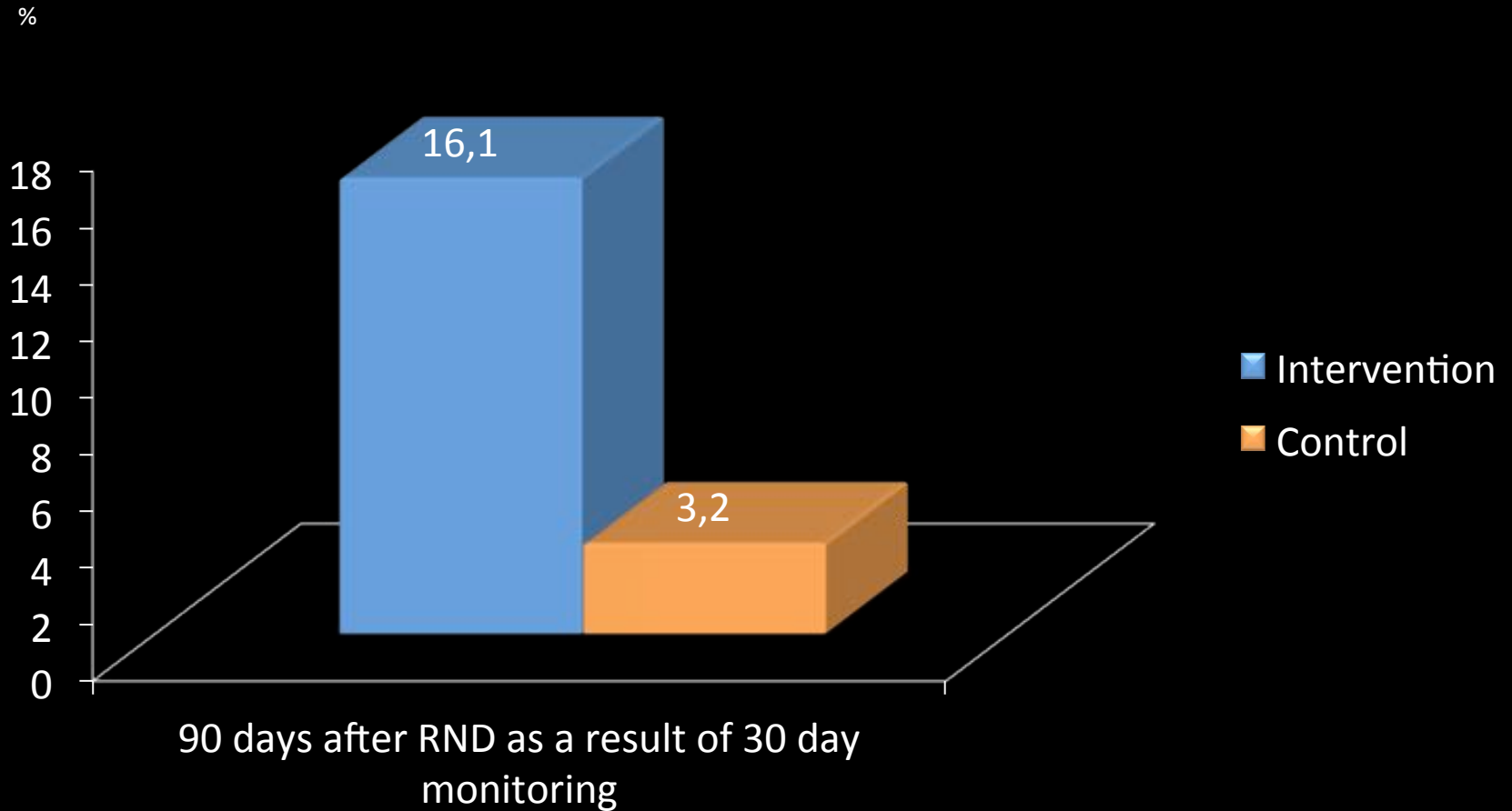
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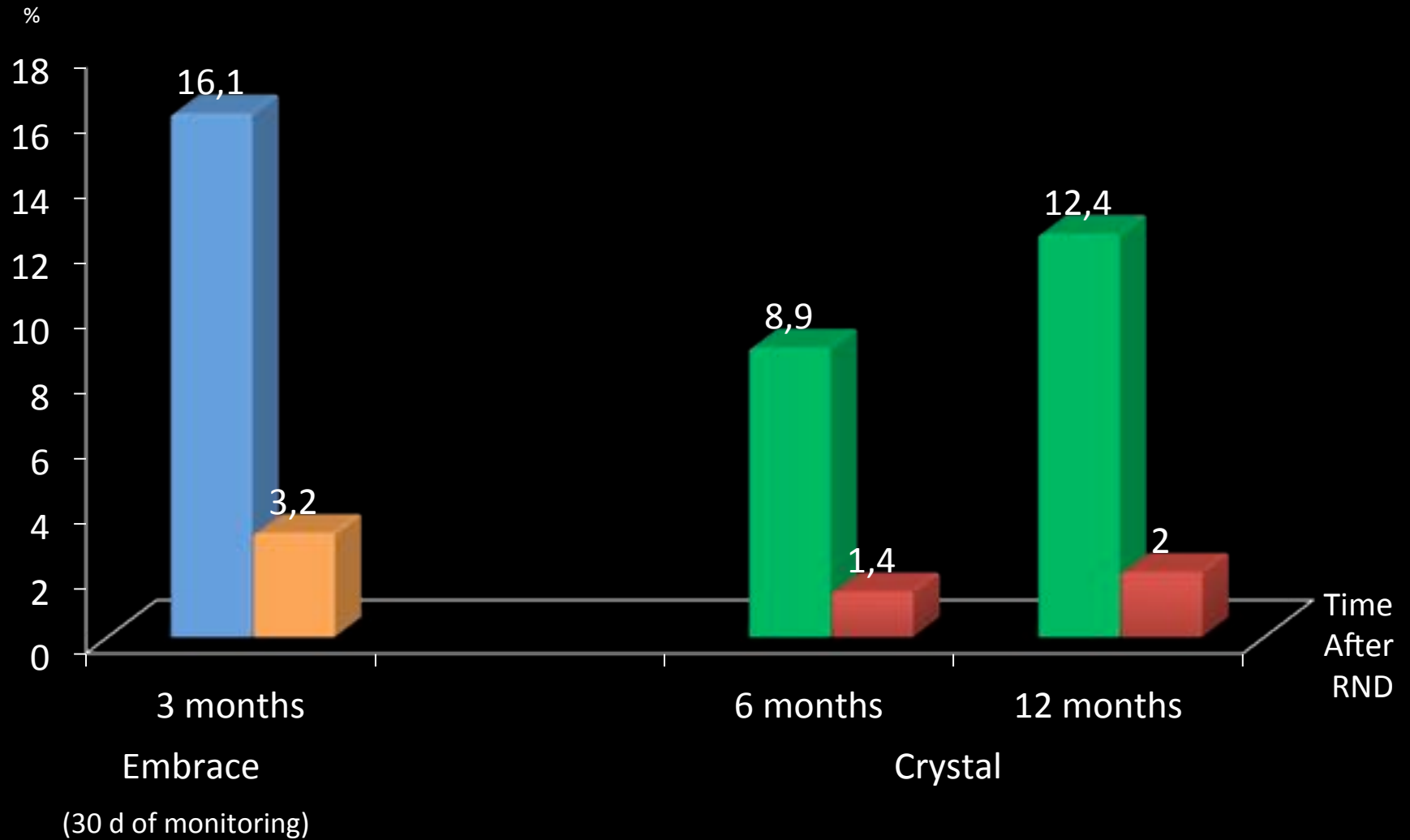
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Atrial fibrillation detection



N Engl J Med 2014;370:2467-77

AF in Embrace vs. Crystal



Mean Age

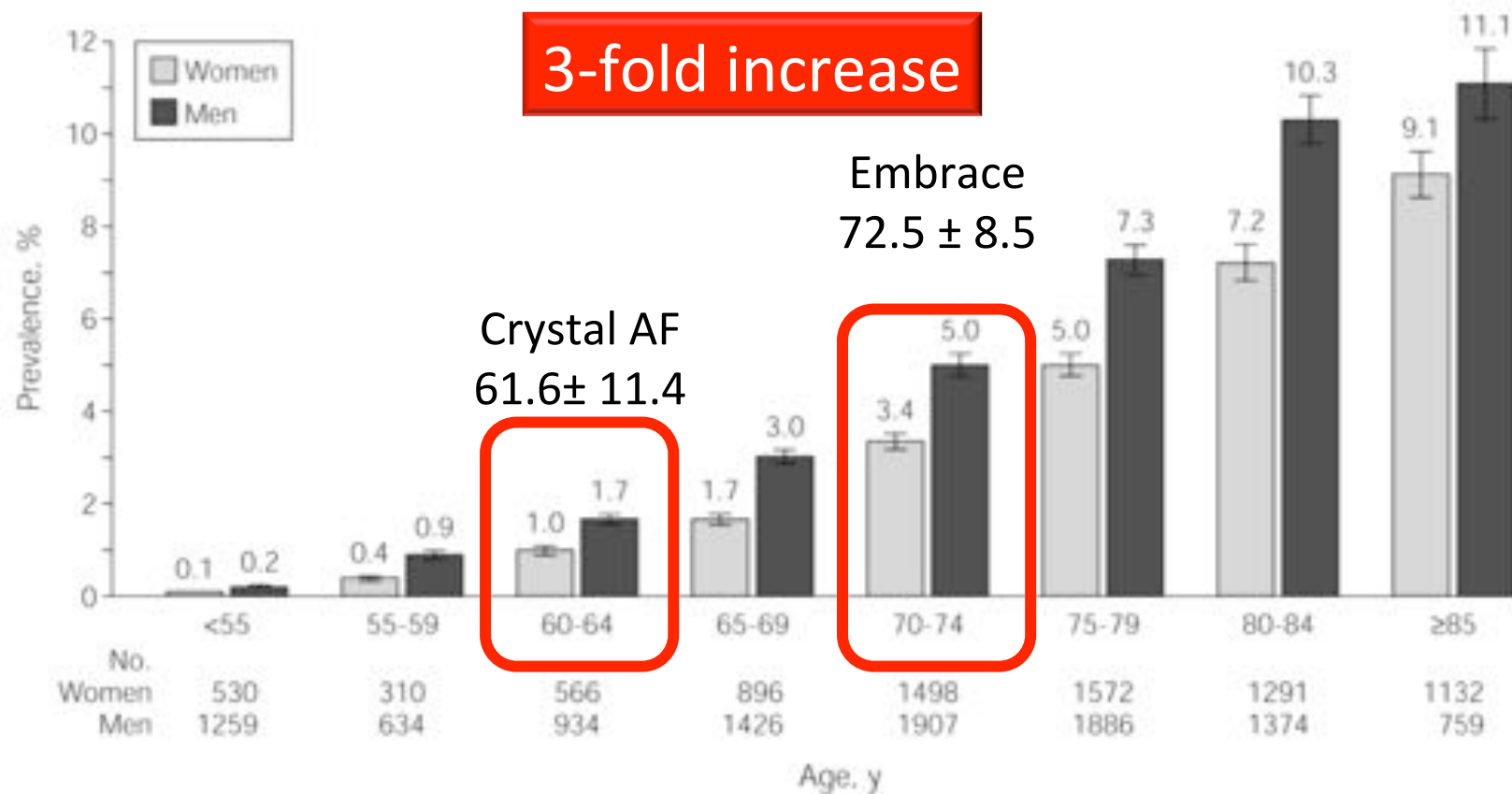
Embrace

Crystal AF

72.5 ± 8.5

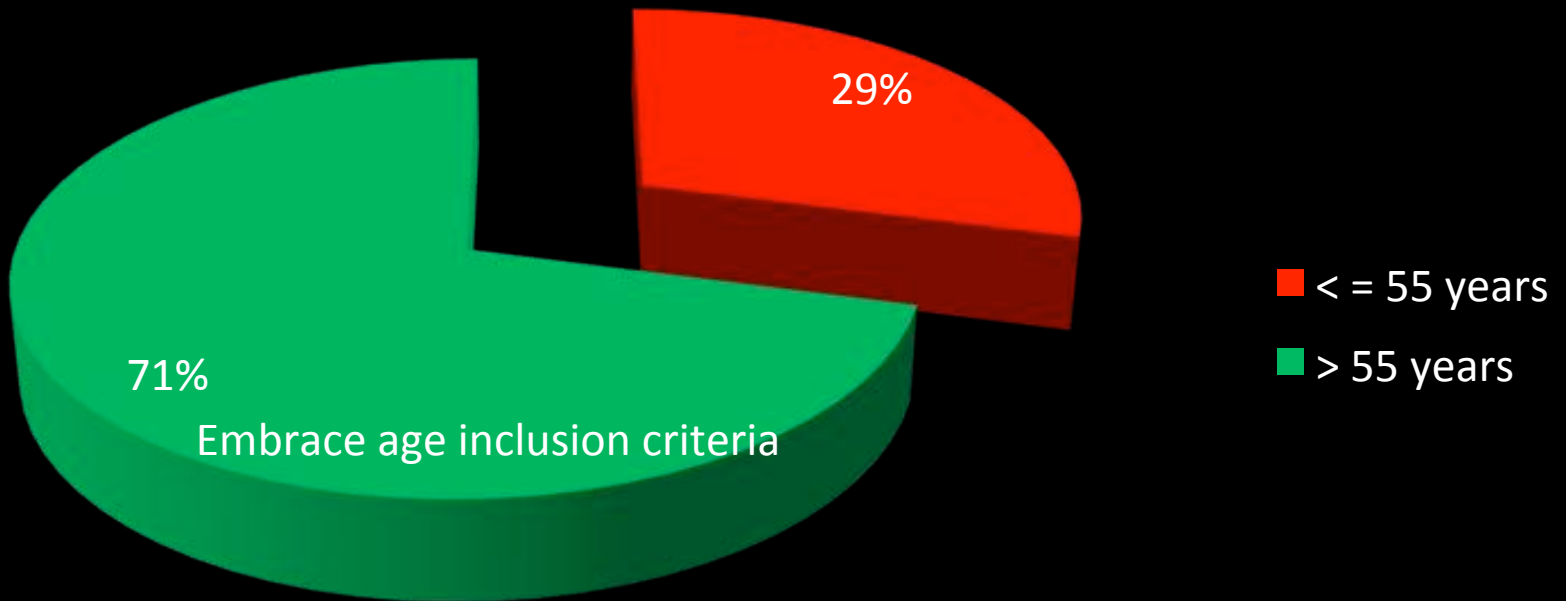
61.6 ± 11.4

Figure 2. Prevalence of Diagnosed Atrial Fibrillation Stratified by Age and Sex



Errors bars represent 95% confidence intervals. Numbers represent the number of men and women with atrial fibrillation in each age category.

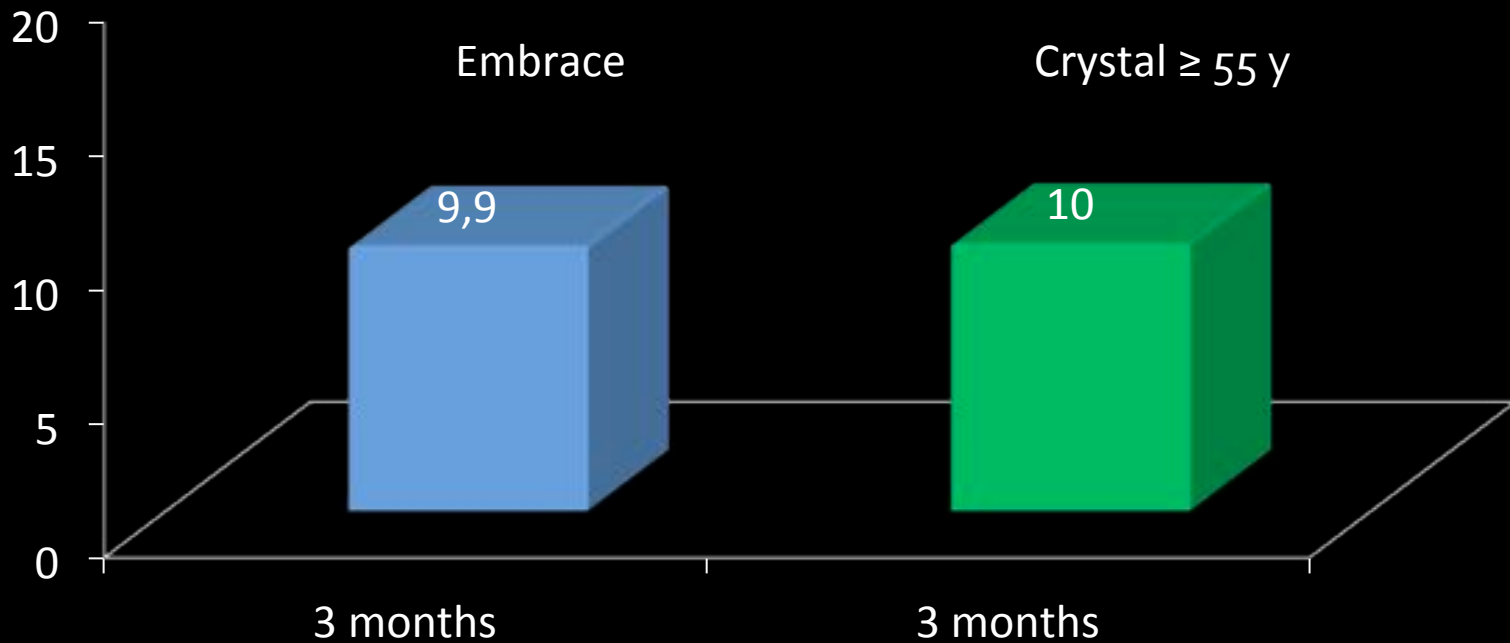
Crystal-AF post hoc analysis



Unpublished data on file

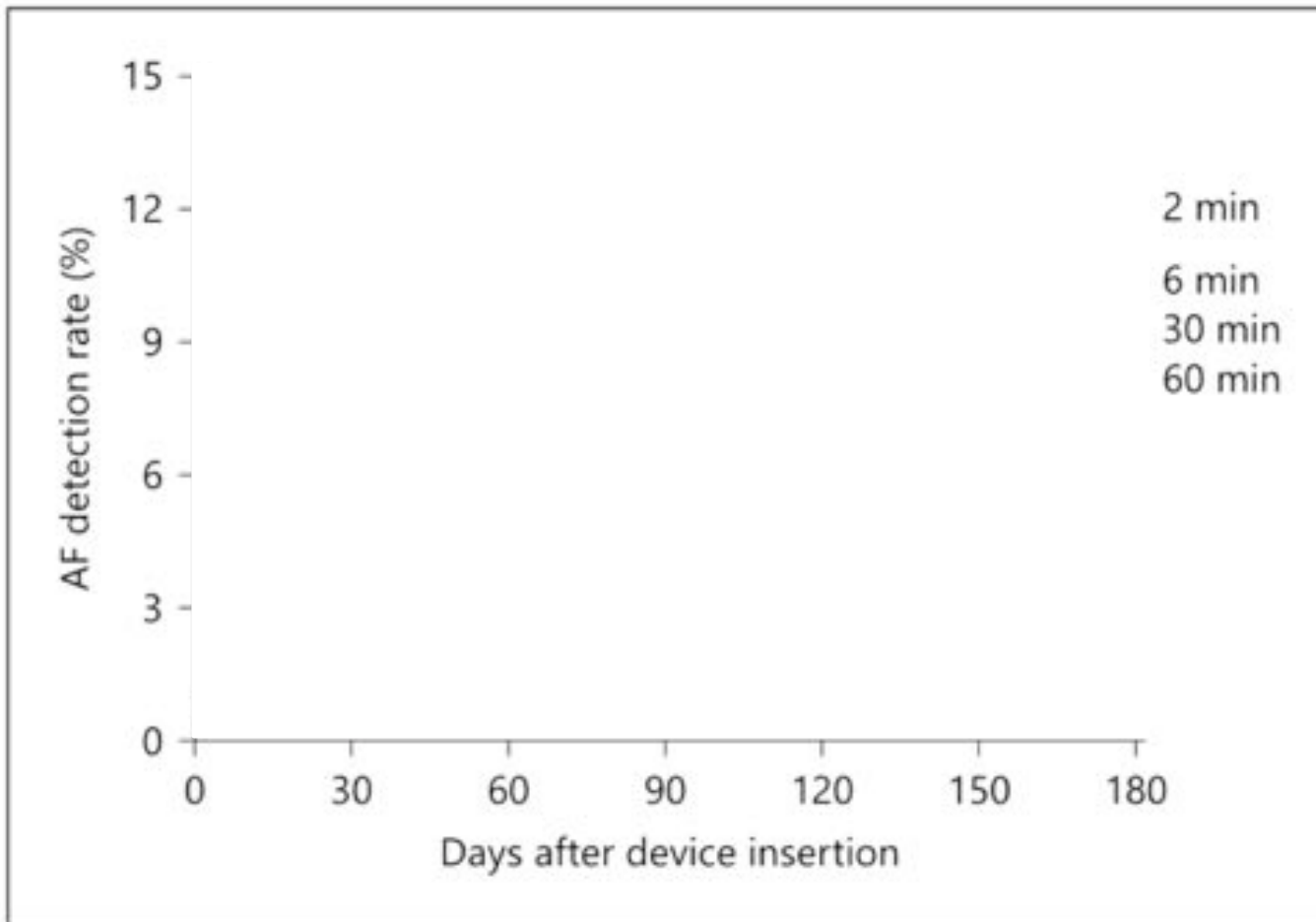
AF in Embrace vs. Crystal ≥ 55 years

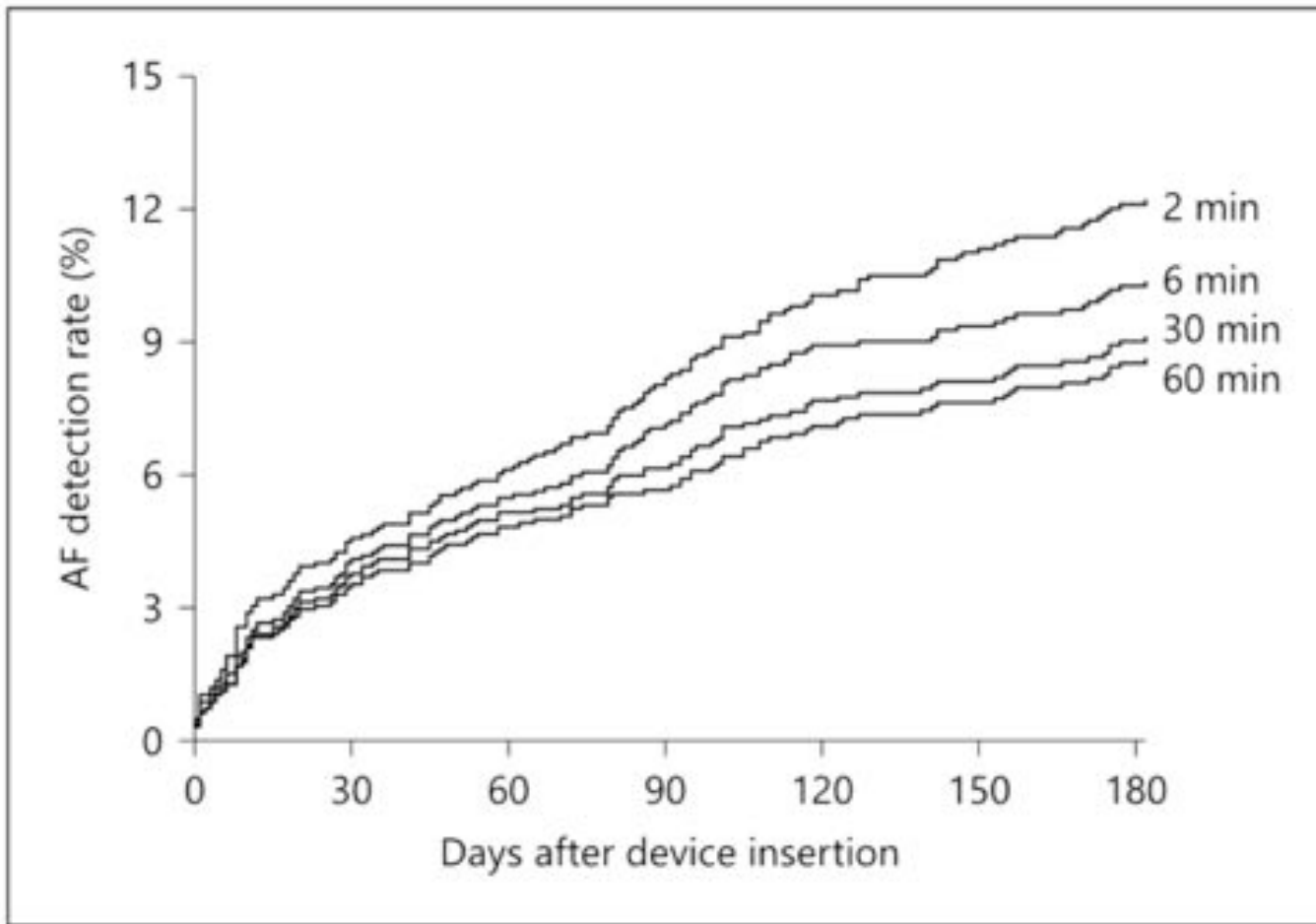
% AF detection rate (episodes of 2.0-2.5 min duration)



Unpublished data on file

2





2

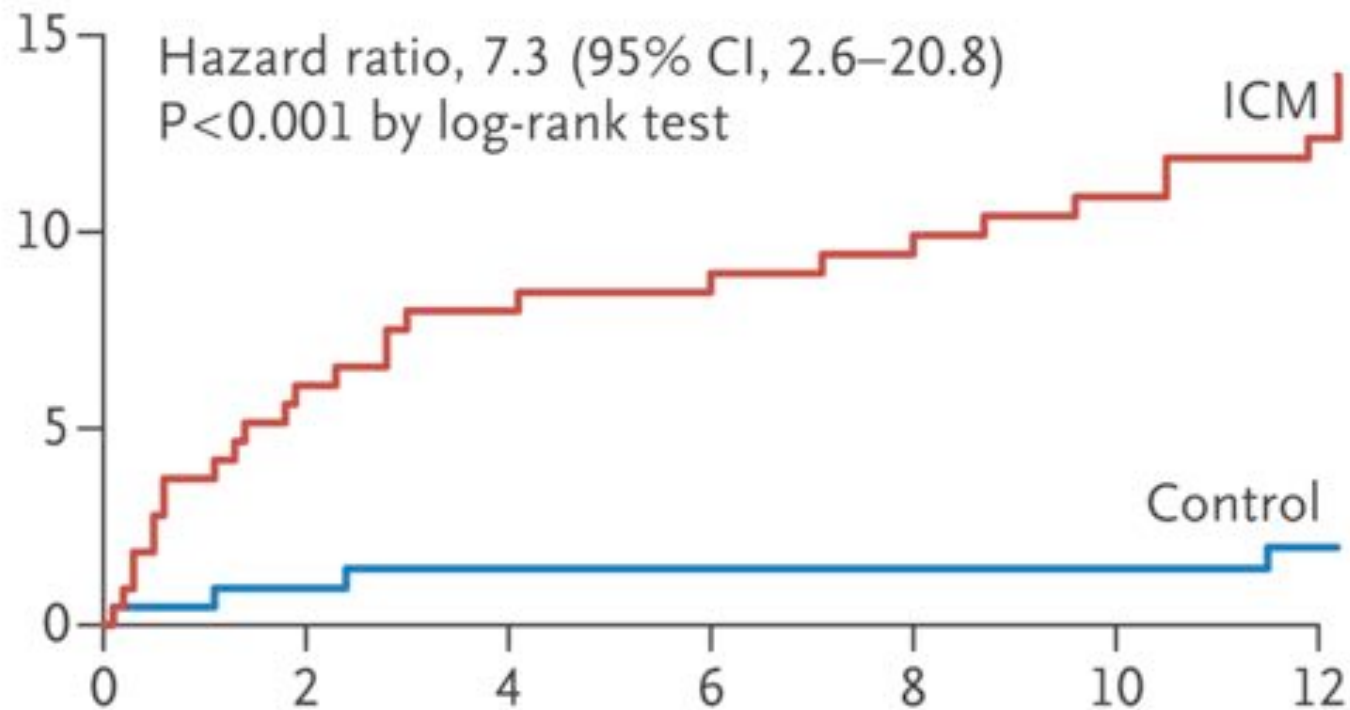
AF episode duration in
endpoint definition

3

A Comparison of Atrial Fibrillation Monitoring Strategies After Cryptogenic Stroke (from the Cryptogenic Stroke and Underlying AF Trial)

William C. Choe, MD^a, Rod S. Passman, MD, MSCE^{b,*}, Johannes Brachmann, MD, PhD^c,
Carlos A. Morillo, MD^d, Tommaso Sanna, MD^e, Richard A. Bernstein, MD, PhD^f,
Vincenzo Di Lazzaro, MD^g, Hans-Christoph Diener, MD, PhD^h, Marilyn M. Rymer, MDⁱ,
Frank Beckers, PhD^j, Jodi Koehler, MS^k, and Paul D. Ziegler, MS^k, for the CRYSTAL AF Investigators

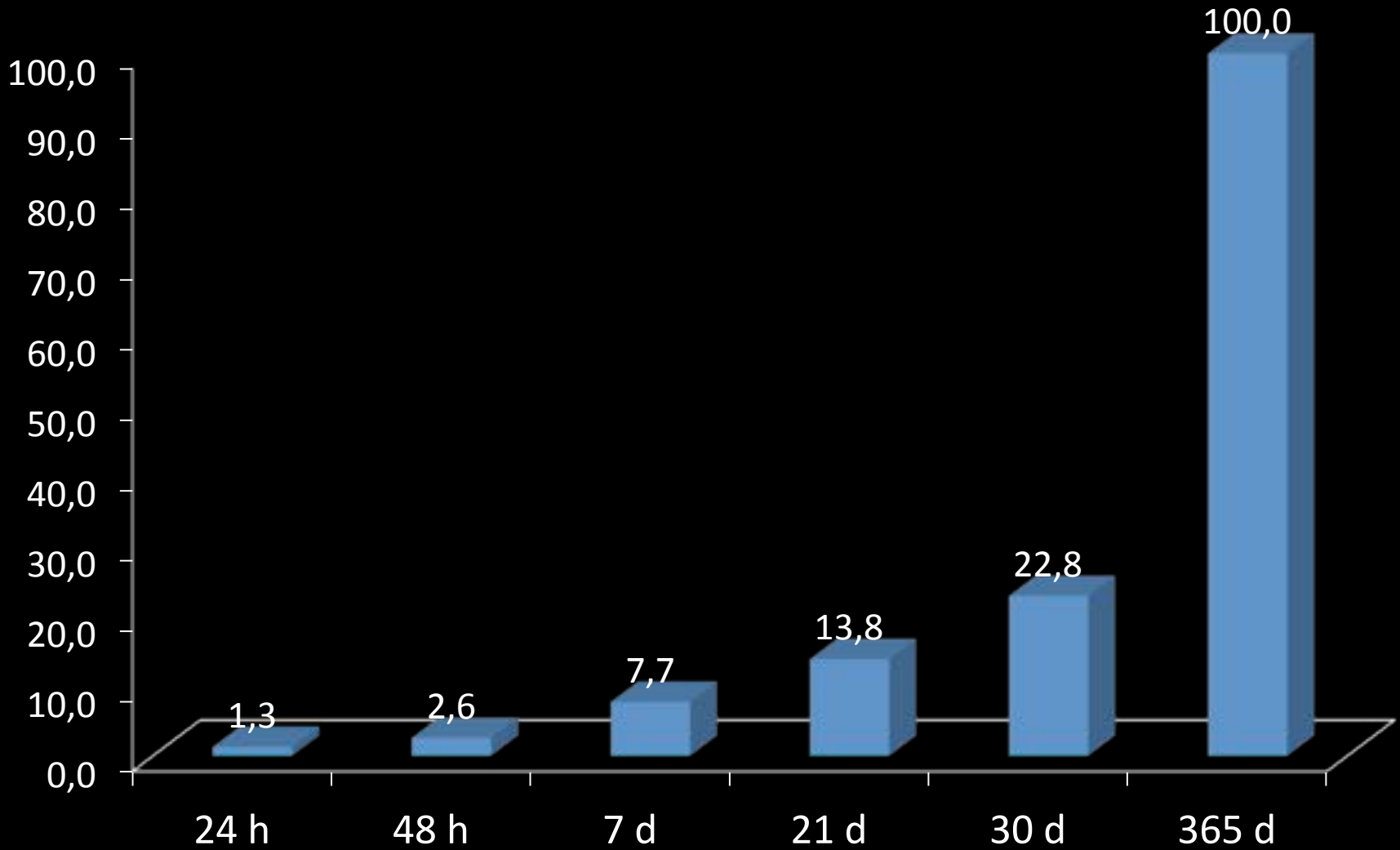
(Am J Cardiol. 2015 Jun 24. pii: S0002-9149(15)01526-X)



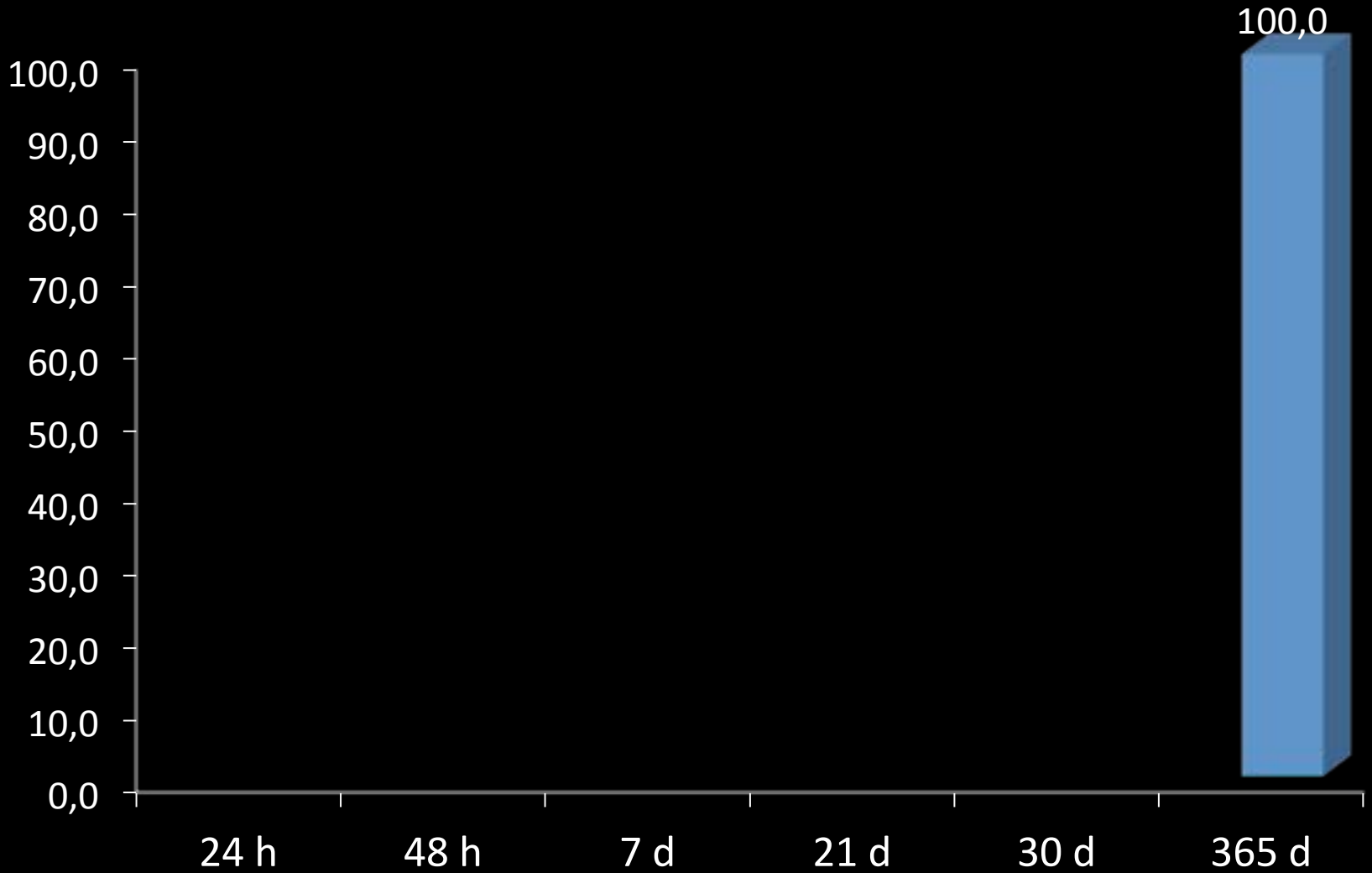
Months since randomization

N Engl J Med 2014;370:2478-86.

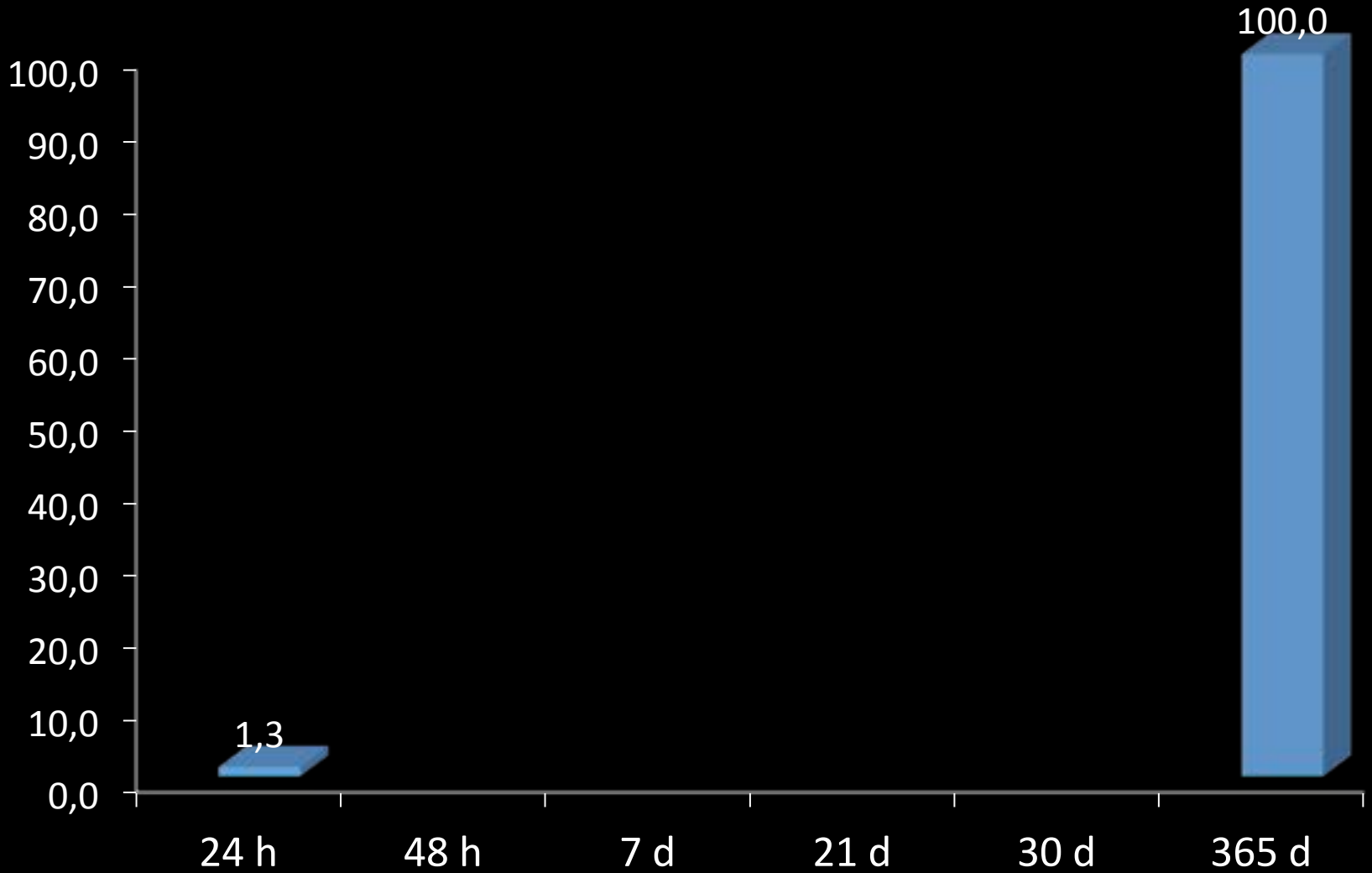
Sensitivity



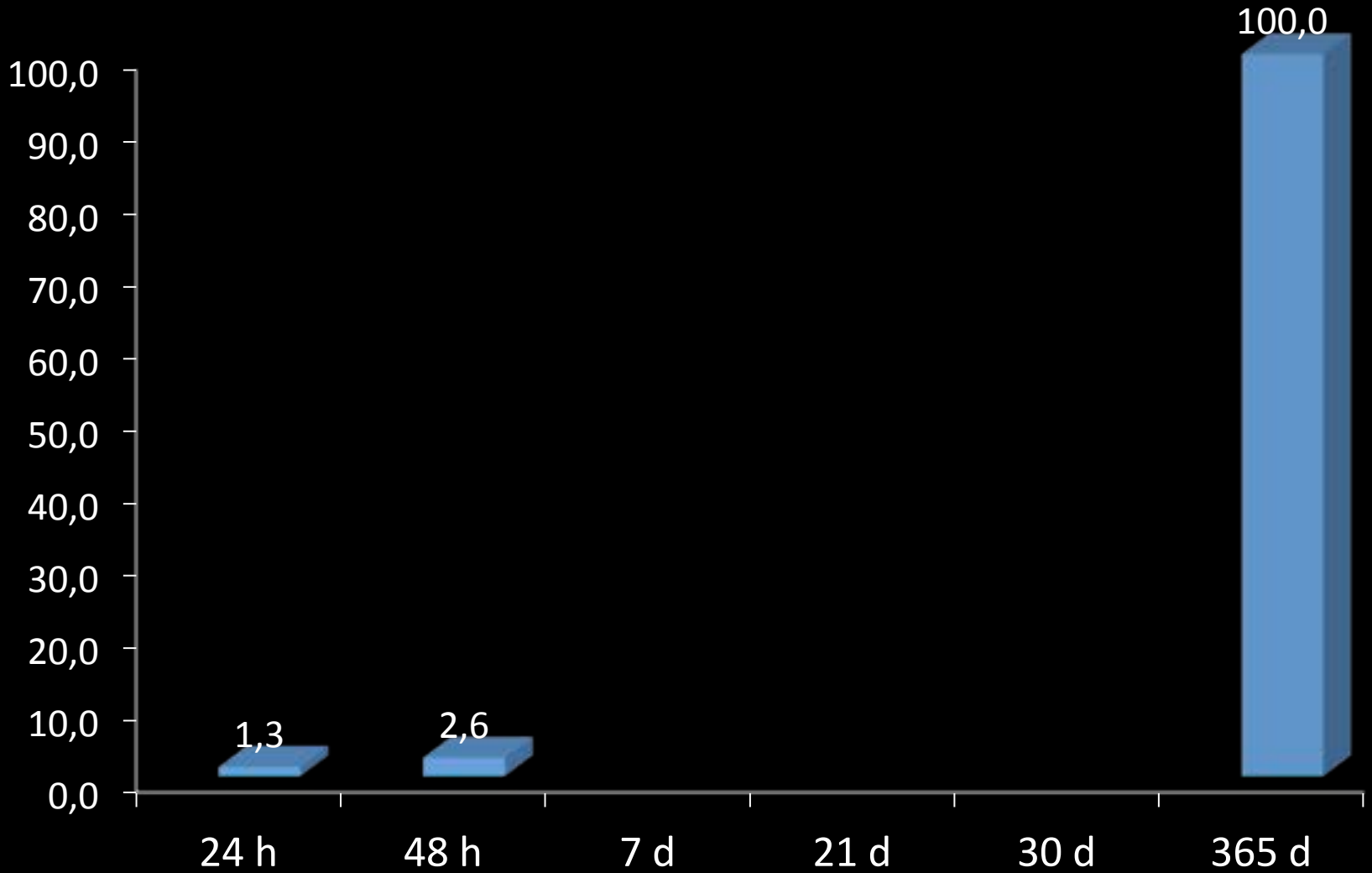
Sensitivity



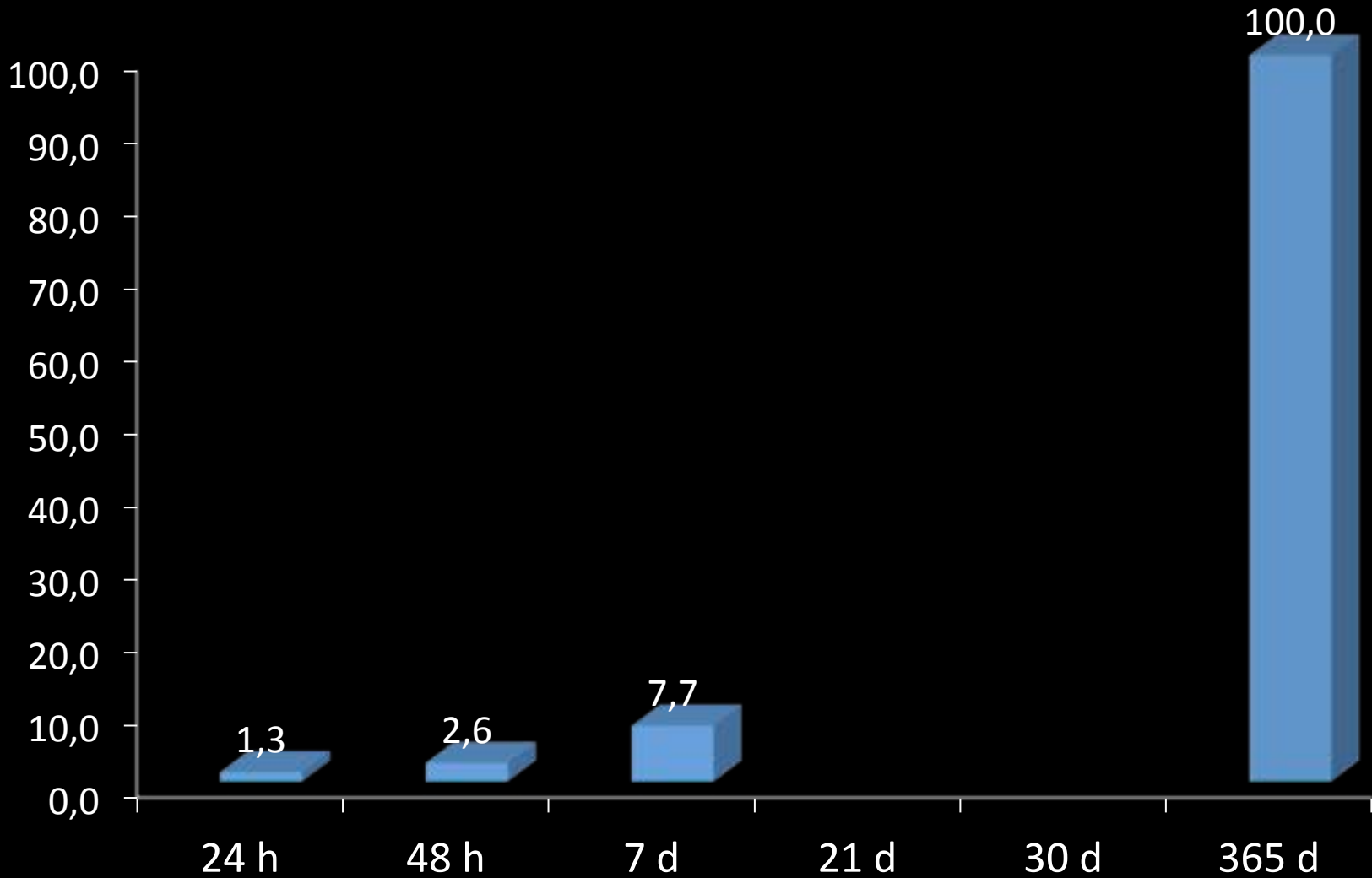
Sensitivity



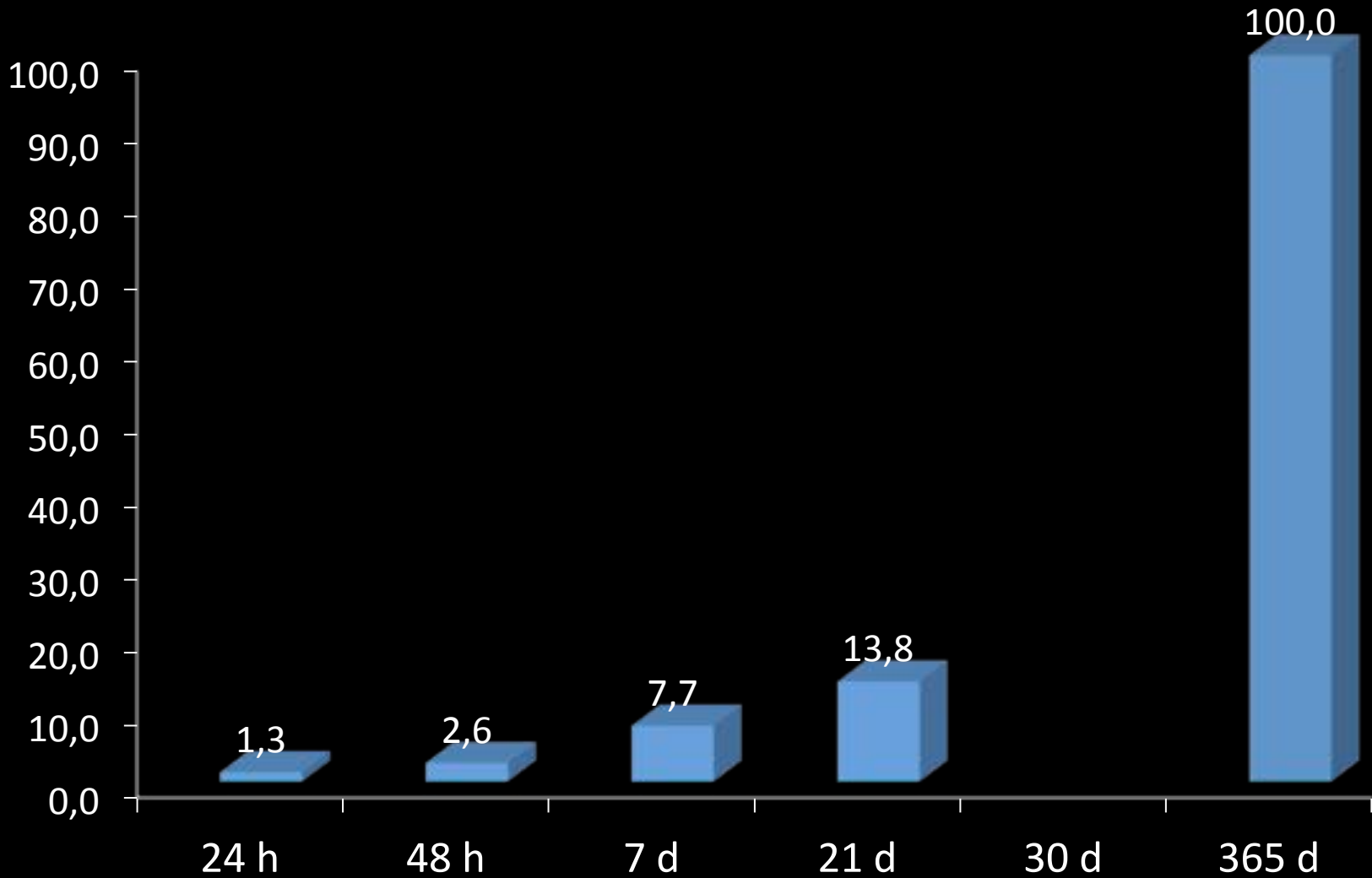
Sensitivity



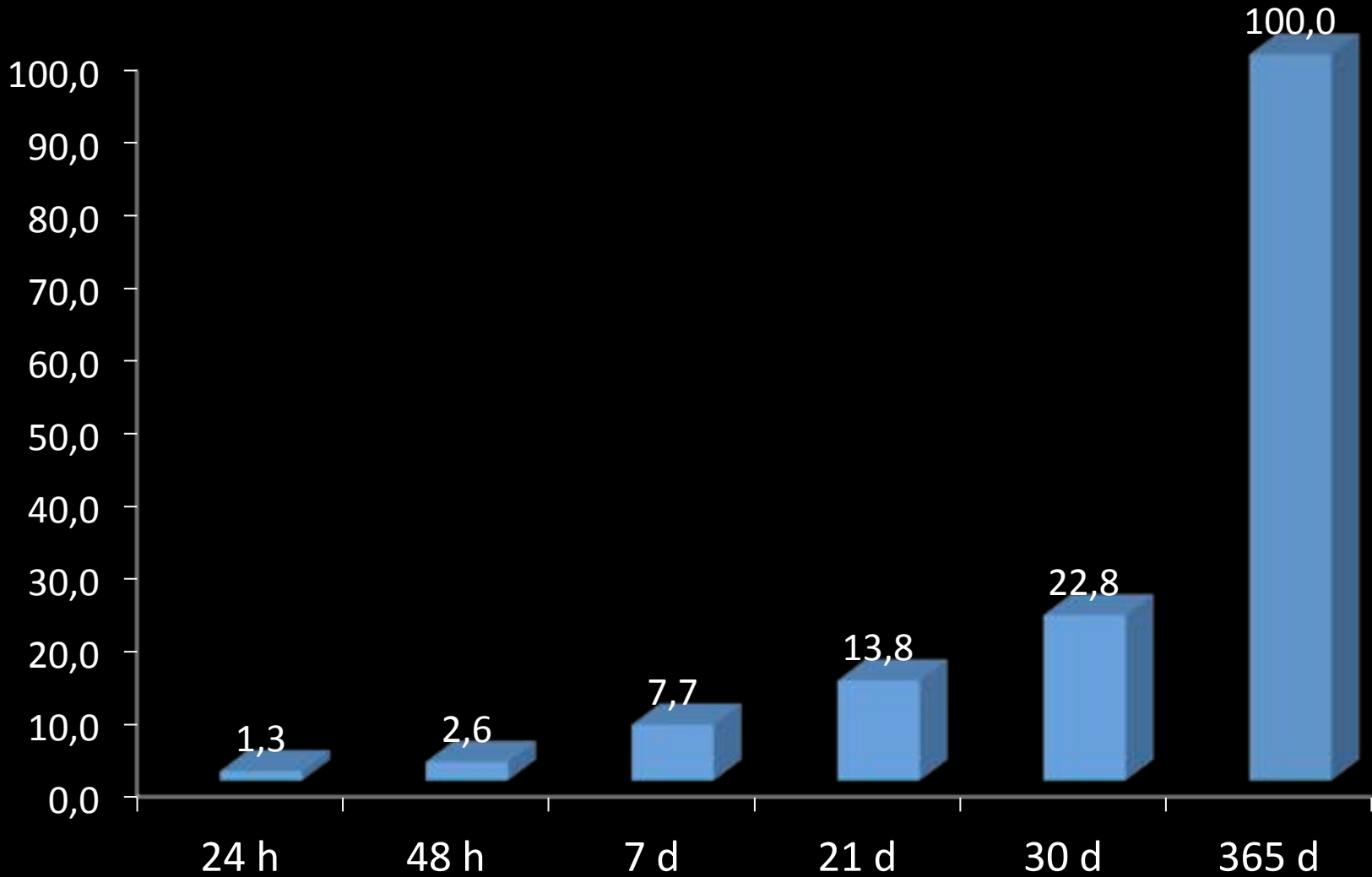
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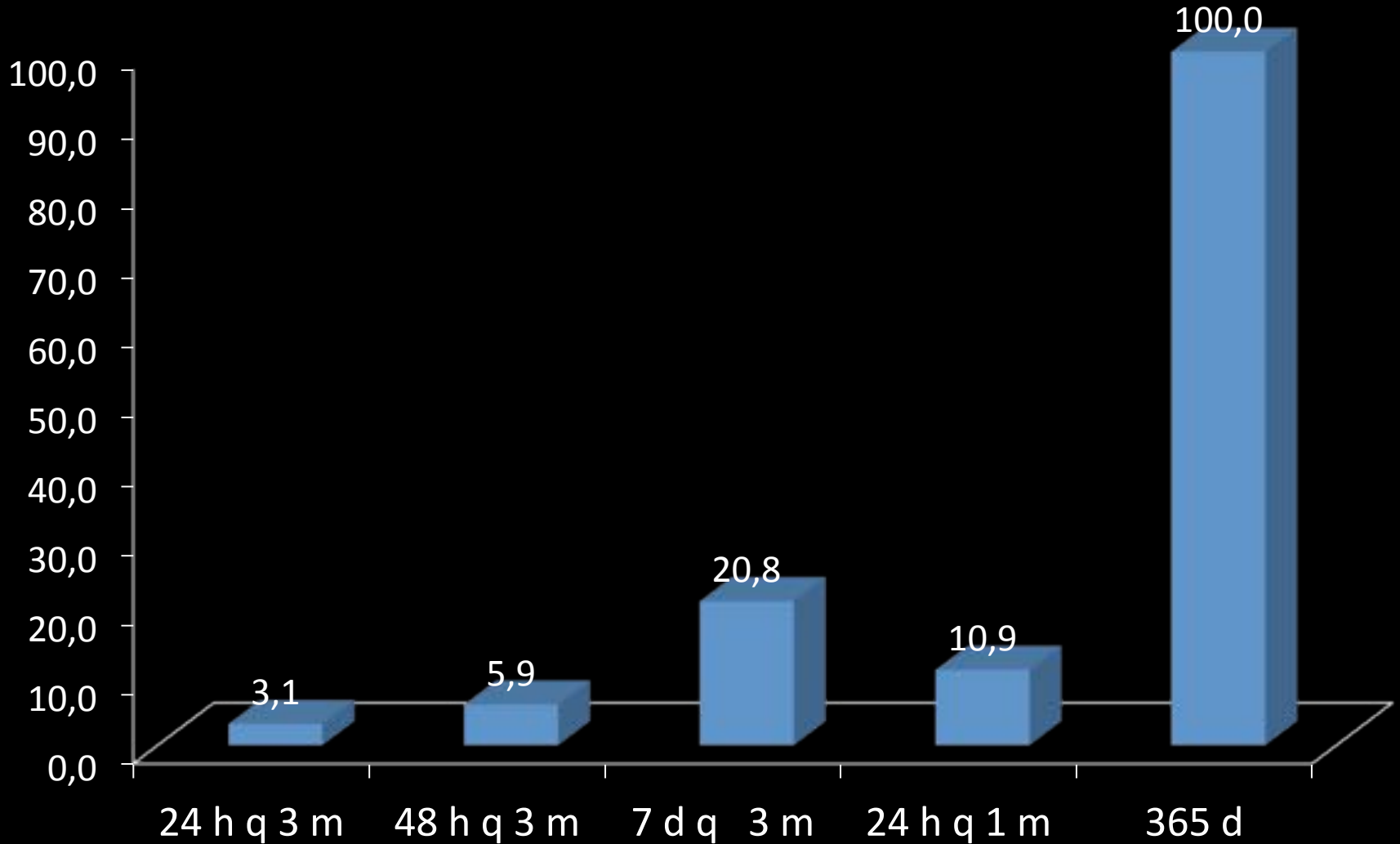
Sensitivity



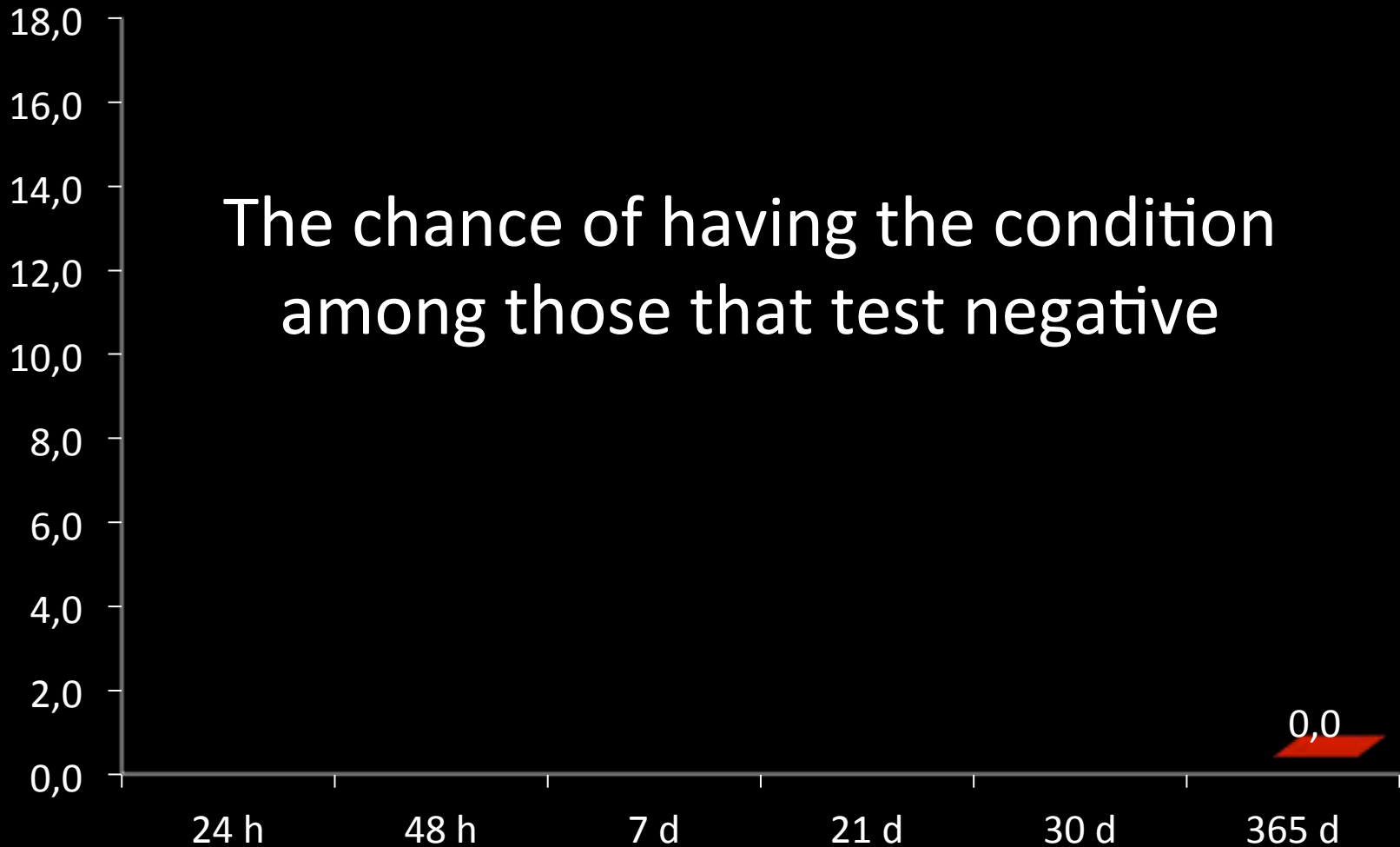
Sensitivity



Sensitivity

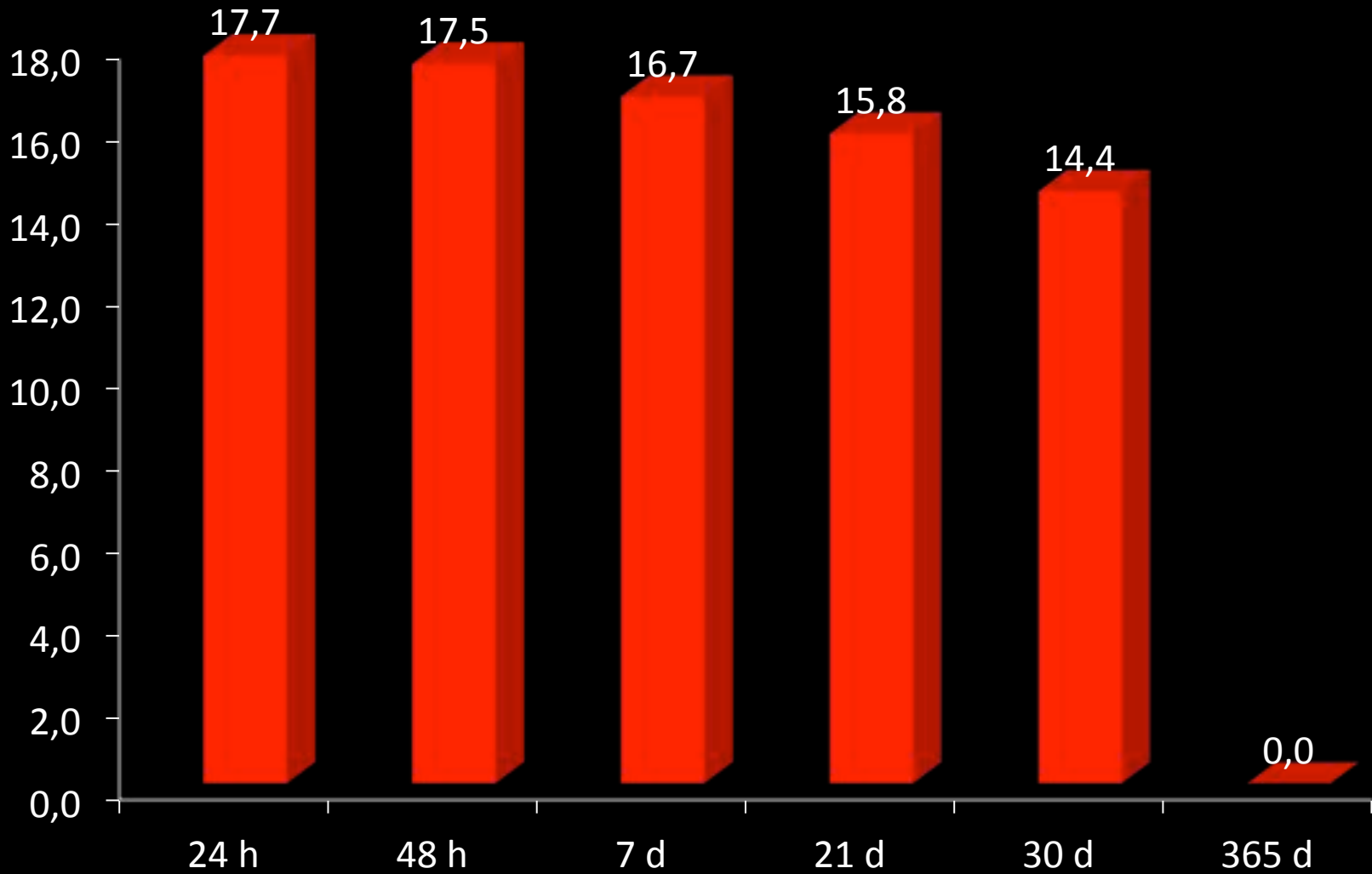


False omission rate



(Modified from: Am J Cardiol. 2015 Jun 24. pii: S0002-9149(15)01526-X)

False omission rate



(Modified from: Am J Cardiol. 2015 Jun 24. pii: S0002-9149(15)01526-X)

3

Duration of monitoring

4

Table 2. Detection of Atrial Fibrillation in the Two Monitoring Groups.

Outcome	Intervention Group (N = 286) <i>number/total number (percent)</i>	Control Group (N = 285) <i>number/total number (percent)</i>	Absolute Difference (95% CI) <i>percentage points</i>	P Value
Primary outcome: detection of atrial fibrillation with duration ≥ 30 sec within 90 days [†]	45/280 (16.1)	9/277 (3.2)	12.9 (8.0–17.6)	<0.001
Secondary outcomes [‡]				
Detection of atrial fibrillation with duration ≥ 30 sec	44/284 (15.5)	7/277 (2.5)	13.0 (8.4–17.6)	<0.001
Detection of atrial fibrillation with duration ≥ 2.5 min	28/284 (9.9)	7/277 (2.5)	7.4 (3.4–11.3)	<0.001
Detection of atrial fibrillation of any duration	56/284 (19.7)	13/277 (4.7)	15.0 (9.8–20.3)	<0.001

What is the AF burden?

Table 2 Detection of Atrial Fibrillation in the Flecainide Group

Duration	Control Group (n = 183)	Flecainide Group (n = 183)	Absolute Difference (95% CI)	P Value
Number of patients with AF (n = 183)	17 (9.3%)	5 (2.7%)	12 (6.6%)	< .001
Duration of AF (min)	26 (14.2%)	2 (1.1%)	24 (13.1%)	< .001
Number of patients with AF with duration ≥ 2.5 min	16 (8.7%)	4 (2.2%)	12 (6.5%)	< .001
Duration of AF with duration ≥ 2.5 min (min)	21 (11.5%)	1 (0.5%)	20 (11.0%)	< .001

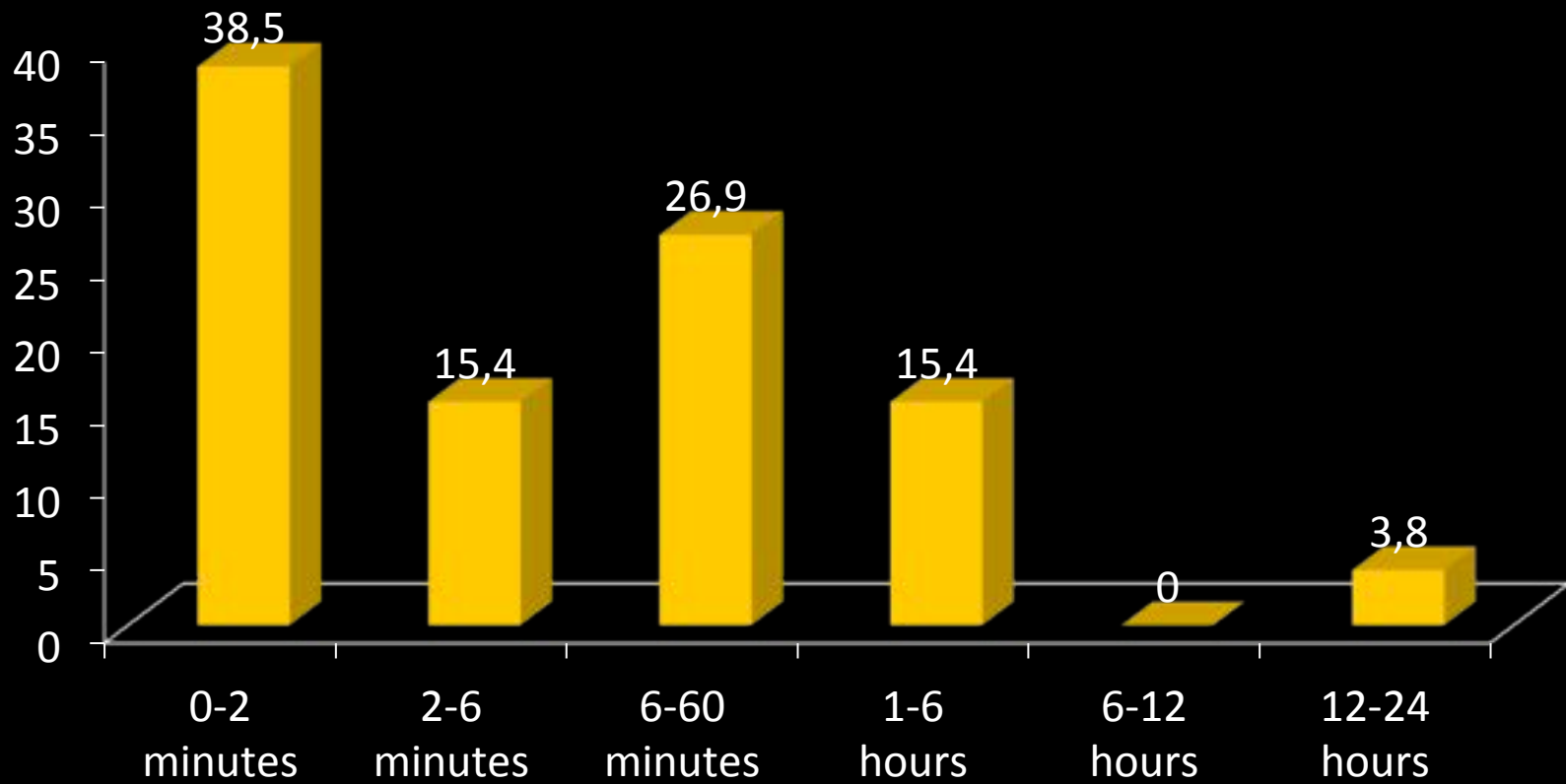
Detection of atrial fibrillation with duration ≥ 2.5 min

Semiquantitative AF duration



Mean AF duration in a single day

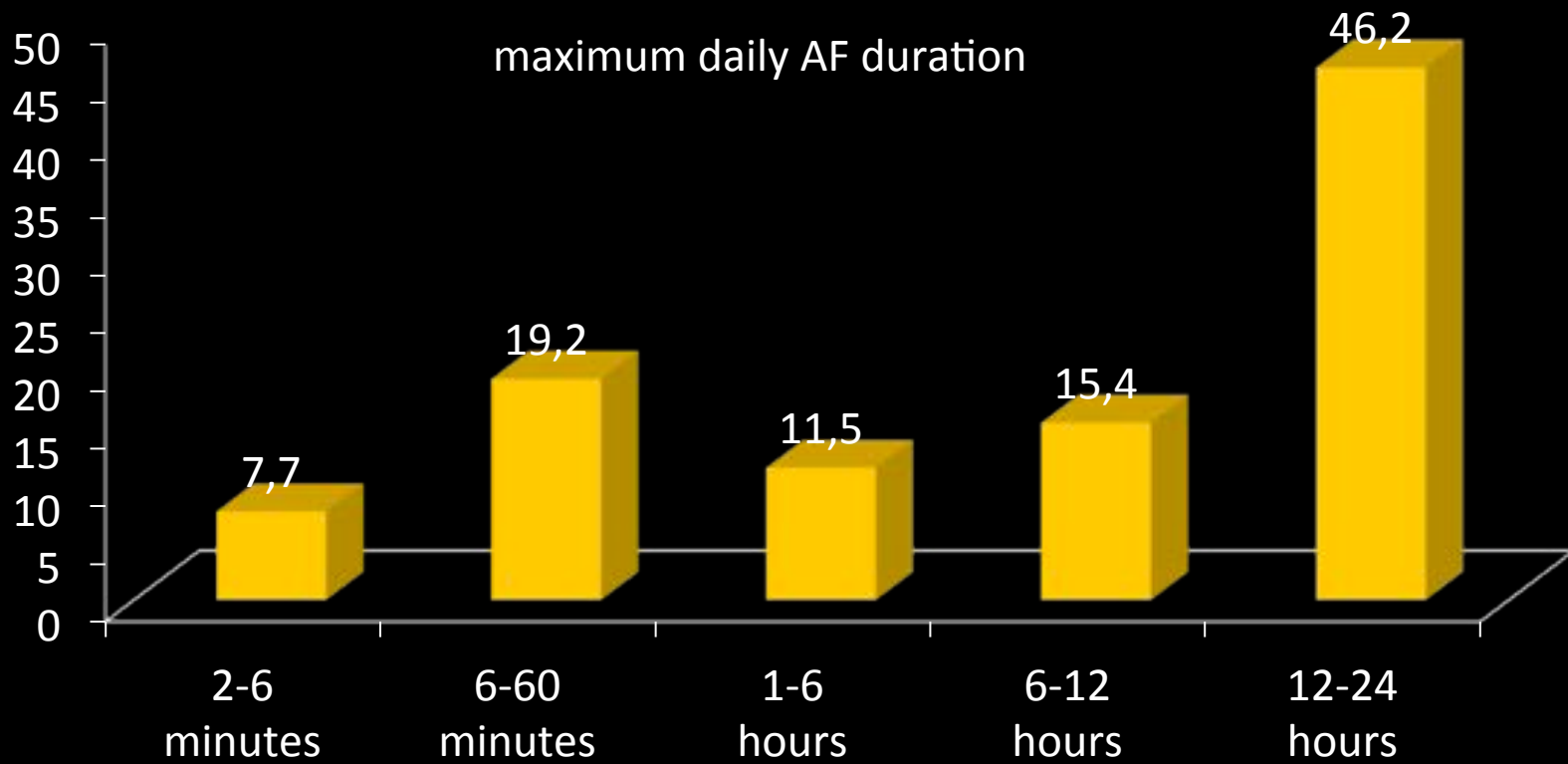
% of patients



N Engl J Med 2014;370:2478-86.

Availability of information to assist decision making

% of patients



N Engl J Med 2014;370:2478-86.

4

Ability to provide
information on AF burden

AF burden and risk of thromboembolism

Table 4 Summary of studies on AF detected by dual-chamber cardiac implantable electronic devices and thromboembolic risk

Year	Trial	No. of patients	Duration of follow-up	Atrial rate cutoff	AF burden threshold	Hazard ratio for TE event	TE event rate (below vs above AF burden threshold)
2003	Ancillary MOST ⁴⁷	312	27 months (median)	> 220 bpm	5 minutes	6.7 (<i>P</i> = .020)	3.2% overall (1.3% vs 5%)
2005	Italian AT500 Registry ⁴⁸	725	22 months (median)	> 174 bpm	24 hours	3.1 (<i>P</i> = .044)	1.2% annual rate
2009	Botto et al ⁵⁰	568	1 year (mean)	> 174 bpm	CHADS ₂ + AF burden	N/A	2.5% overall (0.8% vs 5%)
2009	TRENDS ⁵¹	2486	1.4 years (mean)	> 175 bpm	5.5 hours	2.2 (<i>P</i> = .060)	1.2% overall (1.1% vs 2.4%)
2012	Home Monitor CRT ⁵²	560	370 days (median)	> 180 bpm	3.8 hours	9.4 (<i>P</i> = .006)	2.0% overall
2012	ASSERT ²¹	2580	2.5 years (mean)	> 190 bpm	6 minutes	2.5 (<i>P</i> = .007)	(0.69% vs 1.69%)

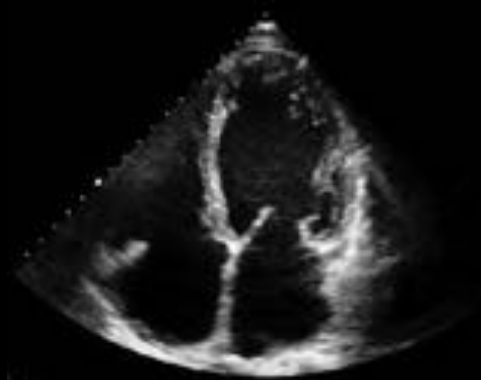
AF = atrial fibrillation; TE = thromboembolic event; N/A = not available.

AF burden and risk of thromboembolism

AF burden threshold	TE event rate (below vs above AF burden threshold)
5 minutes	3.2% overall (1.3% vs 5%)
24 hours	1.2% annual rate
CHADS ₂ + AF burden	2.5% overall (0.8% vs 5%)
5.5 hours	1.2% overall (1.1% vs 2.4%)
3.8 hours	2.0% overall (0.69% vs 1.69%)
6 minutes	

5

Quality of initial work-up



6

Time from event to RND

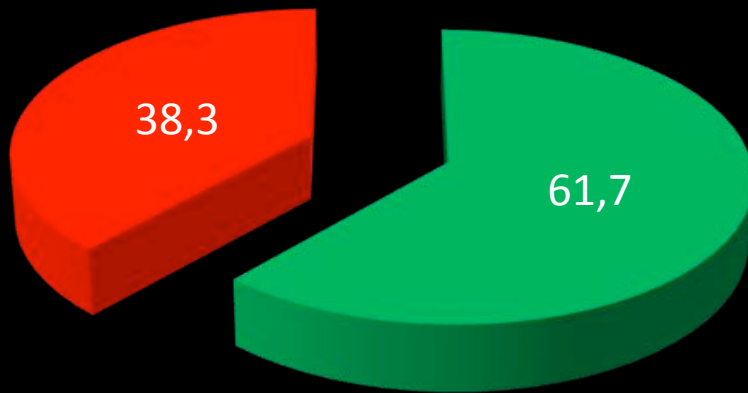


7

Compliance

4 weeks completed

■ Completed ■ Not completed

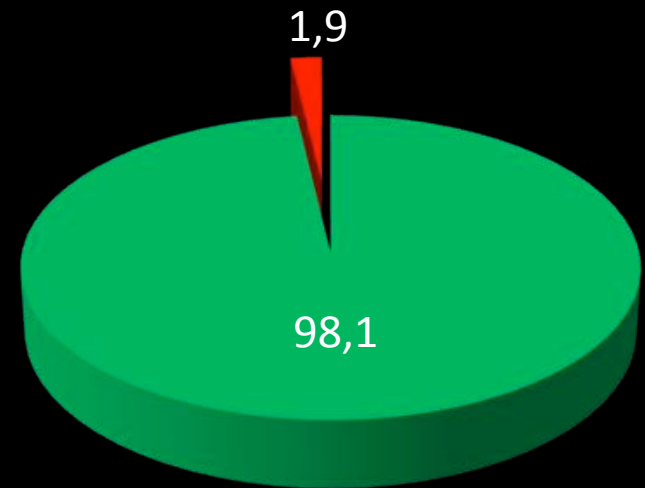


Among pts in whom AF was not detected

Embrace

ICM inserted at 6 months

■ ICM inserted ■ ICM removed



Among pts in whom AF was not detected

Crystal AF

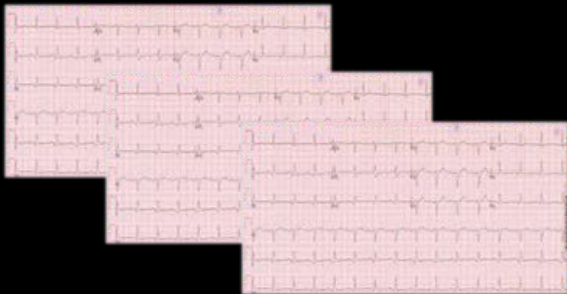
8



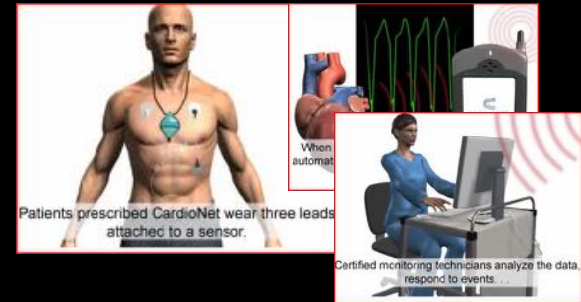
No AF detection algorithms
Storage triggered by high heart rate



AF detection algorithms



CC0 Public Domain



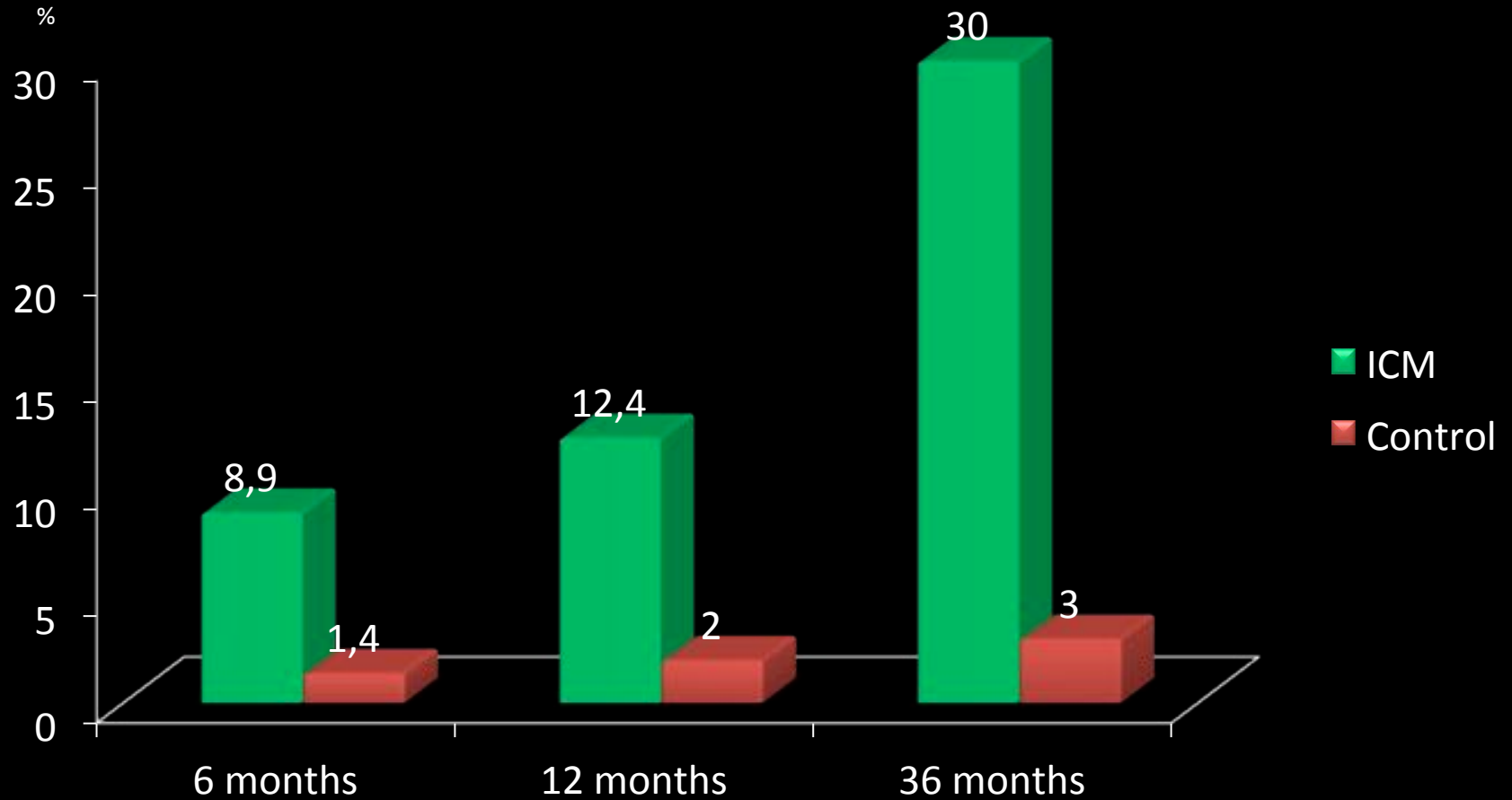


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- https://commons.wikimedia.org/wiki/File:Spot_the_difference.png#/media/File:Spot_the_difference.png

Factors to analyze

1. **AGE** of the study population
2. **AF duration** in **endpoint** definition and independent adjudication
3. **DURATION** of ECG **monitoring**
4. Ability to provide information on **AF BURDEN** to assist decision making (switch to OAC)
5. **WORK-UP** before randomization
6. **TIME** from stroke to monitoring initiation
7. **Compliance**
8. Technology

Crystal AF long term data

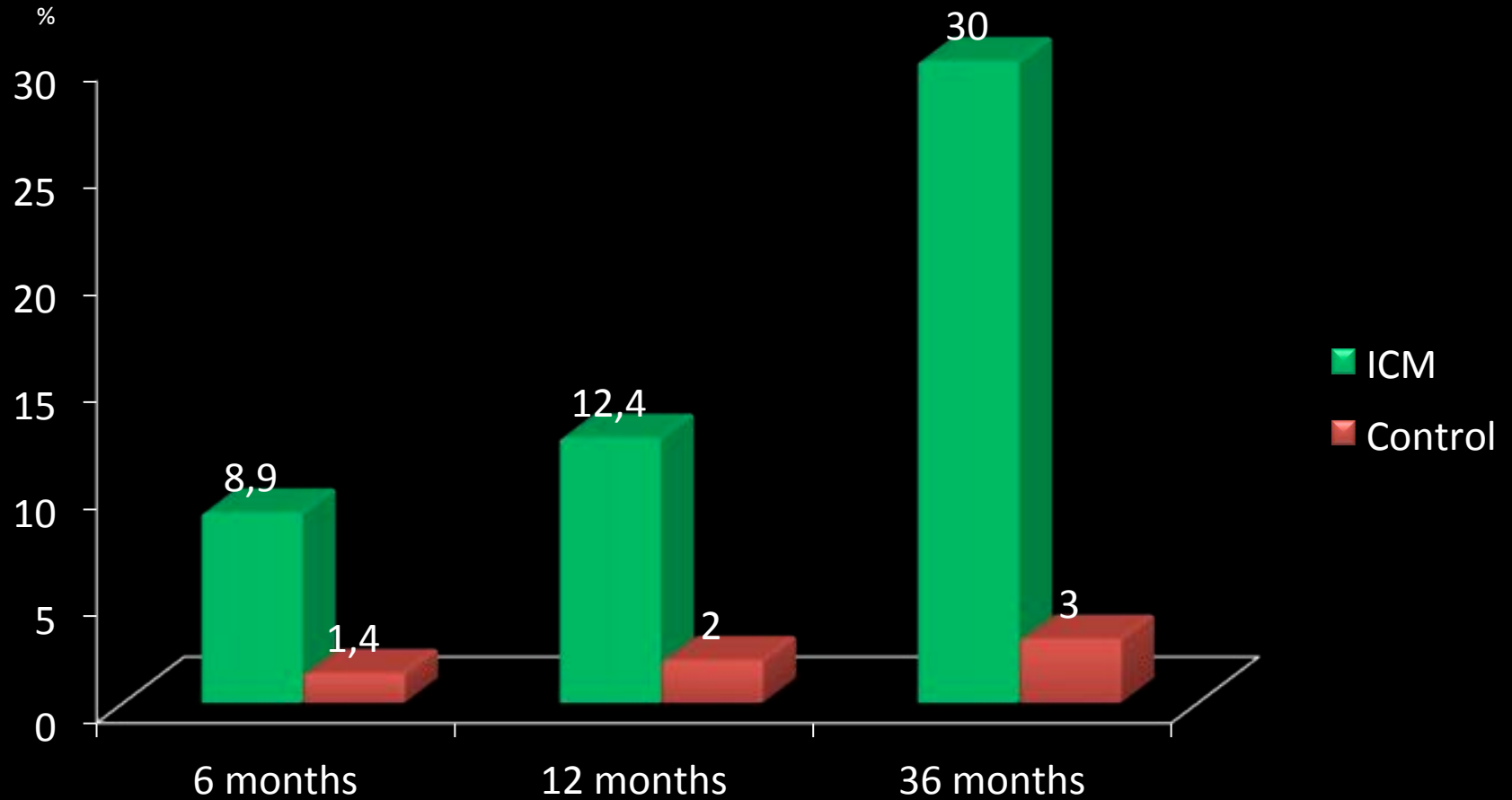


N Engl J Med 2014;370:2478-86.

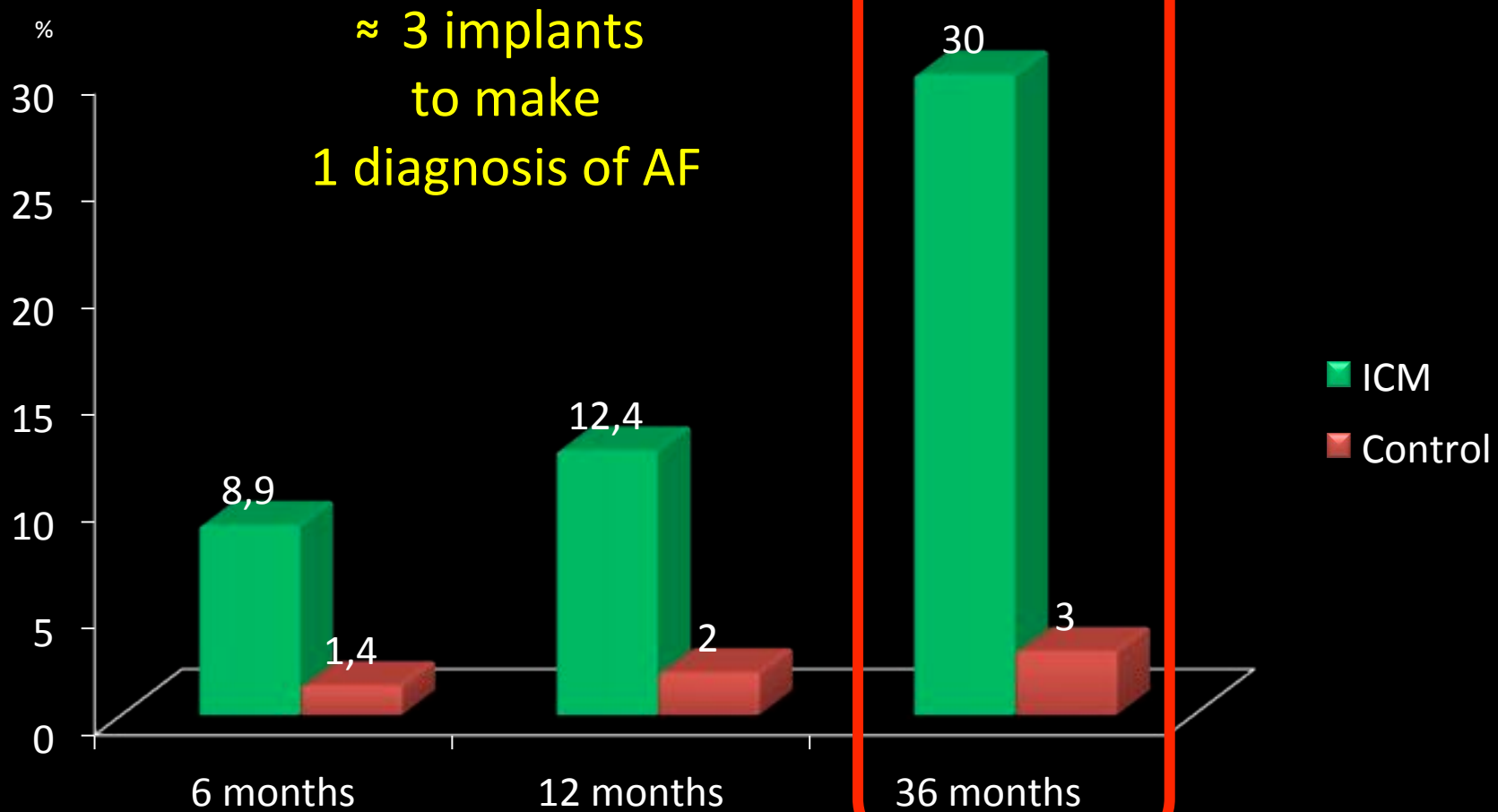
If you find AF **early or late** after an ischemic stroke it doesn't make any practical difference:

in both cases you can **reduce the risk** of stroke recurrence by switching to **oral anticoagulants!**

The longer you monitor the more AF you find



N Engl J Med 2014;370:2478-86.

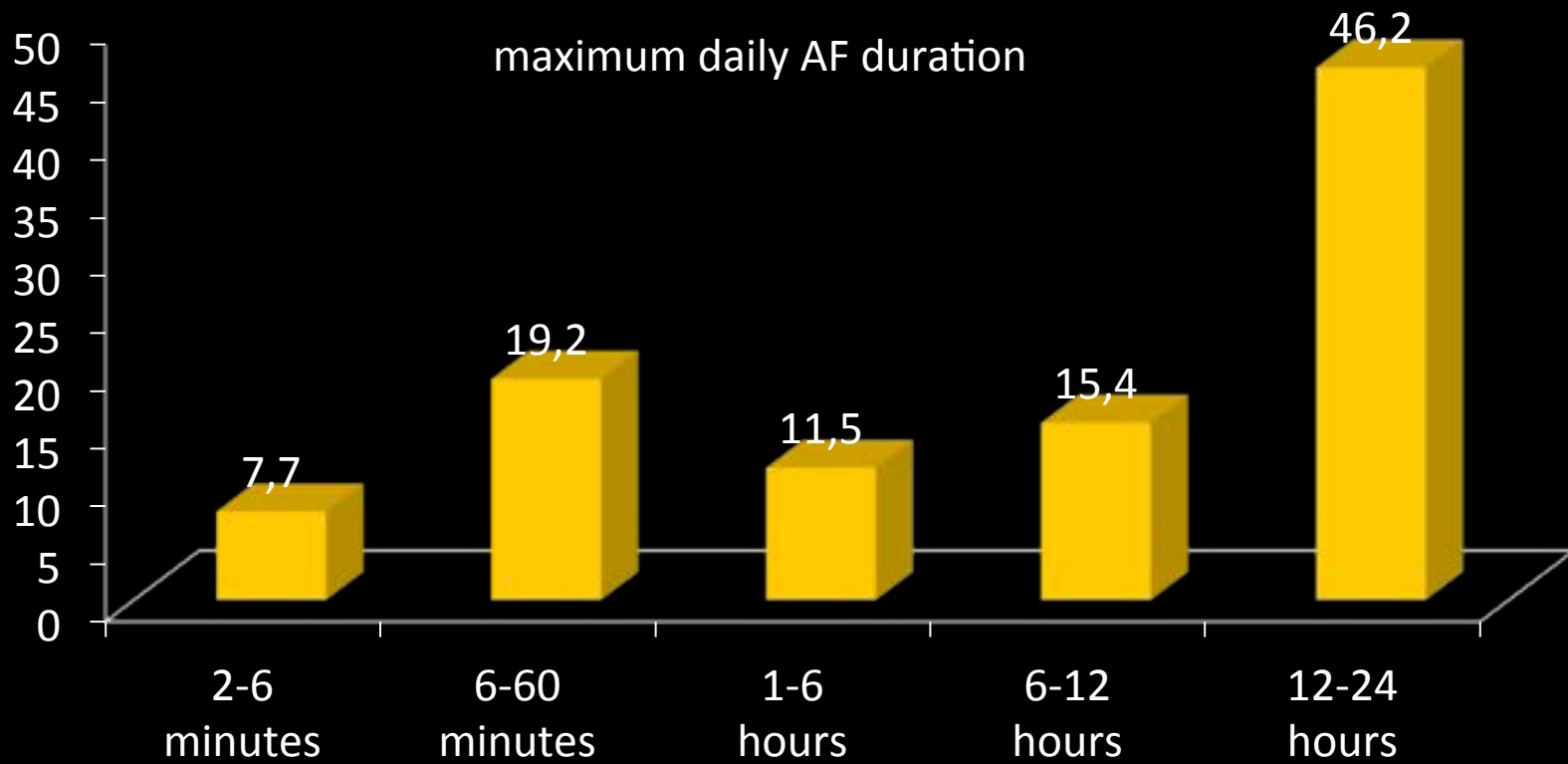


N Engl J Med 2014;370:2478-86.

When comparing costs, consider
the **cost per diagnosis made**

Availability of information to assist decision making

% of patients



N Engl J Med 2014;370:2478-86.

«The longer you monitor
the more AF you find»